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THE FACTOR OF SPASM IN THE ETIOLOGY OF PEPTIC ULCERS

M. E. STEINBERG, M.D.

AND

PAUL H. STARR, B.S.

PORTLAND, ORE.

Exalto [1] was the first investigator to develop a technic which regularly produced chronic ulcerations of the jejunum. He severed the stomach immediately above the pyloric valve according to the method of von Eiselsberg. The distal and proximal ends of the stomach were closed. The jejunum was severed distal to the duodenojejunal flexure, and both ends were closed. The distal jejunum was anastomosed to the stomach near its proximal closed end. The duodenum was anastomosed into the jejunum 20 cm. distal to the gastrojejunal anastomosis, according to the method of Roux, or into the colon (fig. 1). Exalto therefore deserves the credit for the originality in implanting the duodenum into the colon and thus completely diverting the alkaline duodenal contents from the gastrojejunal anastomosis.

Exalto performed a typical gastrojejunal anastomosis in seven dogs according to the method of von Eiselsberg without the short-circuiting operation of Roux. He failed to obtain ulcers in any of the animals.

In four dogs Exalto performed a typical von Eiselsberg exclusion anastomosis and diverted the duodenal contents about 20 cm. from the gastrojejunal anastomosis. He also fed his animals certain amounts of hydrochloric acid. In three of four animals he produced typical jejunal ulcers. In the last three dogs he performed a typical von Eiselsberg exclusion gastro-anastomosis and diverted the alkaline duodenal contents into the colon. He was able to produce typical ulcers of the jejunum in each animal operated on in this manner.

This was the first time that a method was found which produced jejunal ulcers in 100 per cent of the experiments (fig. 1). Unfortunately, Exalto's work does not seem to have been carefully read by investigators in this country. It is also to be regretted that Exalto's

From the Department of Physiology, University of Oregon Medical School.

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1. Exalto, J.: Ulcus jejuni nach Gastroenterostomie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **23**:13, 1911.

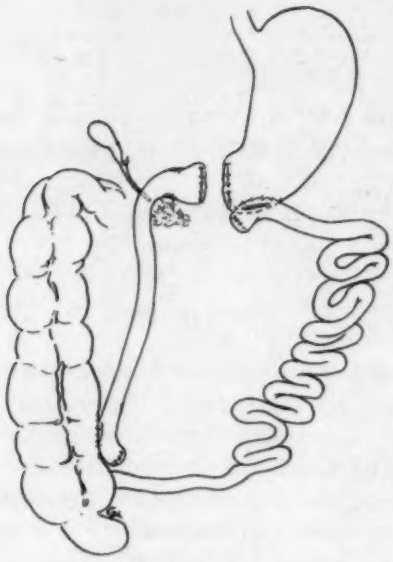

Fig. 1.—A diagram of the method elaborated by Exalto in 1911, which produces ulcers with regularity.

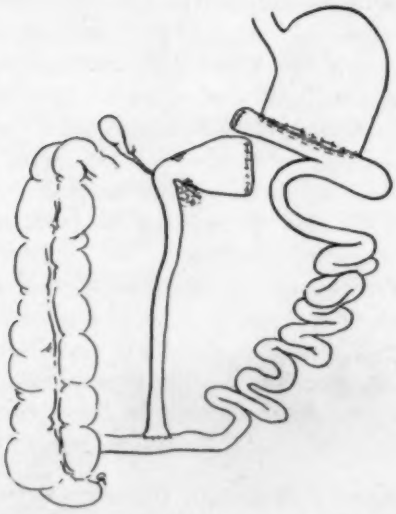

Fig. 2.—A Devine exclusion operation with an Exalto short-circuiting operation which regularly produces ulcers. An entero-anastomosis opposite the gastro-anastomosis releases the spasm and prevents the formation of ulcers.

findings have been erroneously quoted by some (McCann [2] and Matthews and Dragstedt [3]).

In the last few years interest in the etiology of peptic ulcer has been renewed, and many investigators have used the typical Exalto technic or some modification of it. Many have been able to corroborate Exalto's findings (Mann and Williamson,[4] Ivy,[5] Steinberg and Proffitt,[6] Matthews and Dragstedt [3] and others). Winkelbauer [7] repeated Exalto's experiments but divided the stomach in the middle, thus excluding the entire motor part. The duodenal contents were diverted into the lower ileum or the colon (fig. 2). He was able to produce ulcers in every dog operated on in this manner. Steinberg [8] used the same technic as Winkelbauer but diverted the duodenal contents 70 cm. away from the gastrojejunal anatomosis. Definite chronic ulcers of the jejunum developed in 75 per cent of his animals. Matthews and Dragstedt [3] have demonstrated that ulcers of the jejunum are produced under certain conditions with regularity only if the duodenal contents are diverted into the colon or are prevented from finding their way back into the stomach by valve formation. This would offer a probable explanation as to why Steinberg was able to find only 75 per cent of ulcers in his animals.

Winkelbauer has made an attempt to study the relation of the spastic condition of the jejunum anastomosed to the stomach to the genesis of postoperative peptic ulcers. He utilized the method of Kreidel, who demonstrated on dogs that circular and longitudinal muscle layers can be removed from large areas of the stomach and intestine without apparent harm to the dog. The mucosa left after the muscle layers have been stripped off is sufficient protection against perforation. This procedure is somewhat similar to the Weber-Rammstedt operation for hypertrophic stenosis of the pylorus in infants. Winkelbauer used Exalto's method of implantation of the duodenum in the lower part of

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2. McCann, J. C.: Experimental Peptic Ulcer, Arch. Surg. **19**:600 (Oct.) 1929.

3. Matthews, W. B., and Dragstedt, L. R.: The Etiology of Gastric and Duodenal Ulcers, Surg., Gynec. & Obst. **55**:265 (Sept.) 1932.

4. Mann, F. C., and Williamson, C. S.: The Experimental Production of Peptic Ulcer, Ann. Surg. **77**:409 (April) 1923.

5. Ivy, A. C.: Factors Concerned in Determining the Chronicity of Ulcers in the Stomach and the Upper Intestine: Susceptibility of Jejunum to Ulcer Formation; Effect of Diet on Healing of Acute Gastric Ulcers, Am. J. Surg. **11**:531, 1931.

6. Steinberg, M. E., and Proffitt, J. C.: The Etiology of Postoperative Peptic Ulcers, Arch. Surg. **25**:819 (Nov.) 1932.

7. Winkelbauer, A.: Studien ueber die Verhütung des Ulcus pepticum postoperativum im Experiment, Arch. f. klin. Chir. **143**:649, 1926.

8. Steinberg, M. E.: The Exclusion Operation for Duodenal Ulcers, Am. J. Surg. **23**:137 (Jan.) 1934.

the ileum or the large bowel, excluding the motor part of the stomach similar to that suggested by Devine for duodenal ulcer (fig. 2). Winkelbauer also stripped the longitudinal and circular muscles of the jejunum anastomosed to the stomach for a distance of from 15 to 25 cm. Only two of the dogs survived from thirty-four to seventy days. In none of the animals was an ulcer demonstrated. In our opinion these experiments did not prove anything conclusively, since a total of two negative findings may easily be considered as a mere coincidence. Nevertheless, we deemed the speculations of Winkelbauer of interest and importance, and extended and augmented his experiments in various ways.

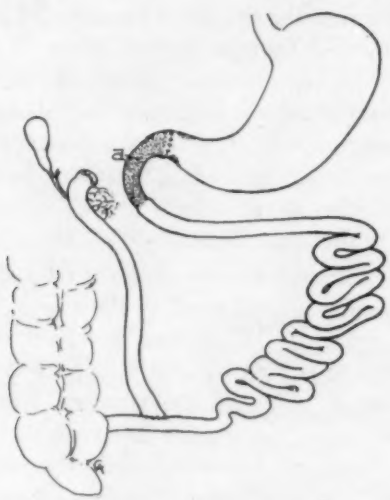

Fig. 3.—An Exalto short-circuiting operation and an end-to-end anastomosis between the pyloric valve and the jejunum. Ulcers formed regularly in from 90 to 100 per cent of the experiments. No ulcers were found where the muscle layer was stripped (*a*).

EXPERIMENTS

Type 1.—Numerous investigators have diverted the alkaline duodenal contents into the ileum or the cecum, according to the method of Exalto, and anastomosed the jejunum to the pyloric valve end-to-end. Acute or chronic ulcers occurred with regularity (Mann and Williamson,[4] Ivy,[5] Steinberg and Profitt,[6] Matthews and Dragstedt[3] and others). Seven of our animals operated on according to the aforementioned method have survived from five to sixty-nine days, and acute or chronic ulcers of the jejunum developed in each. Using these seven animals as controls, we operated on another series of animals, diverting the duodenal contents into the ileum and anastomosing the pyloric valve to the jejunum, as in the control animals, but in addition we stripped the longitudinal and circular muscle of the jejunum for a distance of about 10 cm., beginning at the pyloric valve (fig. 3). By our method a narrow strip of muscle is left at the mesenteric border for the

preservation of the blood supply. Since the jejunum is anastomosed to the pyloric valve end-to-end, before the stripping takes place, a small circular part of the jejunal muscle is left intact near the pylorus. There also results a small triangular area of jejunum covered by muscle near the mesenteric border at the gastrojejunal anastomosis. The stripping of the muscle is easily performed by splitting the muscle wall longitudinally with a knife and then separating it with the finger covered with gauze or by cutting over a spread mosquito forceps which is introduced between the muscle layers and the submucosa. Apparently no harm results from this procedure; the hemorrhage is easily controlled by the application of hot, moist sponges. At postmortem examination hair mixed with débris was occasionally found in the loop stripped of its muscle. The omentum completely covered the jejunal area (fig. 5).

Of several animals operated on according to the aforementioned method, ten survived from seven to seventy-six days. Eight dogs were observed for a period

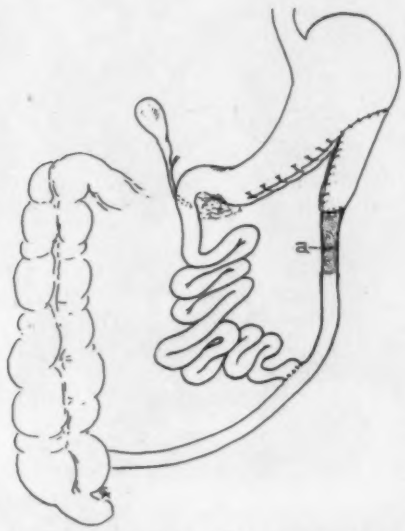

Fig. 4.—An anastomosis between a Pavlov stomach pouch and the ileum according to Matthews and Dragstedt. Ulcers formed in 100 per cent of the experiments. No ulcers occurred where the muscle was stripped (*a*).

of from twenty-one to seventy-six days. In the control experiments in which the muscle was not stripped, this type of experiment produced ulcers in 100 per cent of the animals in about the same period of observation. In none of the ten dogs in which the muscle of the jejunum was stripped did any ulcers develop in the area of the mucosa, where three fourths of the circumference of the longitudinal and circular muscles was stripped. In dog 145 there was a small chronic ulcer near the pyloric valve. The ulcer, however, was surrounded with a part of the jejunal wall, its muscle layers intact (fig. 5). A small chronic ulcer also developed in dog 152, in the jejunum near the pyloric valve. This ulcer was also surrounded by the jejunal wall, with its muscle layers intact. A large ulcer with a deep crater penetrating into the surrounding structures developed in dog 146 (fig. 4). This ulcer began at the mesenteric border where the muscle layers of the jejunum were intact and then penetrated into the neighboring mucosa where the muscle

layers were stripped. The most interesting observations in these experiments were the finding of acute and chronic ulcerations in the jejunum exactly where the muscle layer began its normal intact course, or about 10 cm. from the pyloric valve (figs. 5 and 7). This is, according to our knowledge, the first time that such an observation has been recorded. It was also interesting to notice that the lumen of the jejunum where the muscle wall was stripped was larger than the part of the jejunum where the muscle wall was intact (figs. 5, 6 and 7).

Dog 145 was observed for seventy-four days. We have already recorded the finding of a small chronic ulcer near the pyloric valve, but in addition there was a narrow ulcer about 15 cm. long, beginning exactly where the muscle layer began its normal intact course and therefore separated from the ulcer at the pylorus by a distance of 10 cm.

Dog 152 was observed for forty-eight days. In addition to a small ulcer near the pylorus, already recorded, there were two small chronic typical "kissing ulcers"

Fig. 5.—A gastro-anastomosis (*a*) between the stomach and the jejunum with an Exalto short-circuiting operation (fig. 3). The area between the arrows shows where the muscle layer was stripped from the jejunum. A small ulcer near the pyloric valve and two chronic "kissing ulcers" exactly where the muscle layer begins its intact course, or about 10 cm. from the pyloric valve, are seen. On the peritoneal surface (*b*) of the same specimen the omentum covers the area in which the muscle is stripped.

in the mucosa located exactly where the muscle layer began its intact course, and therefore likewise about 10 cm. distal to the pyloric valve (fig. 5).

Dogs 149 and 144 lived from seven to ten days. No ulcerations were found near the pylorus or in the mucosa of the jejunum where the muscle was stripped. On the other hand, in each of the dogs, at a distance of 10 cm. from the pylorus, exactly where the muscle began its intact course, there were acute defects. A narrow ulcer, 1 cm. in length, following a longitudinal course (dog 144, fig. 7) and a smaller one (dog 149) were found. None of the ten dogs observed from seven to seventy-six days had ulcerations in the area in which the muscle was stripped.

Type 2.—Winkelbauer formed a large Pavlov pouch and anastomosed various parts of the small intestine to the pouch. He was successful in producing an ulcer in the ileum. Matthews and Dragstedt have performed similar operations but also diverted the passage of the intestinal contents from the anastomosis between the pouch and the small intestine. Where the ileum was anastomosed to the

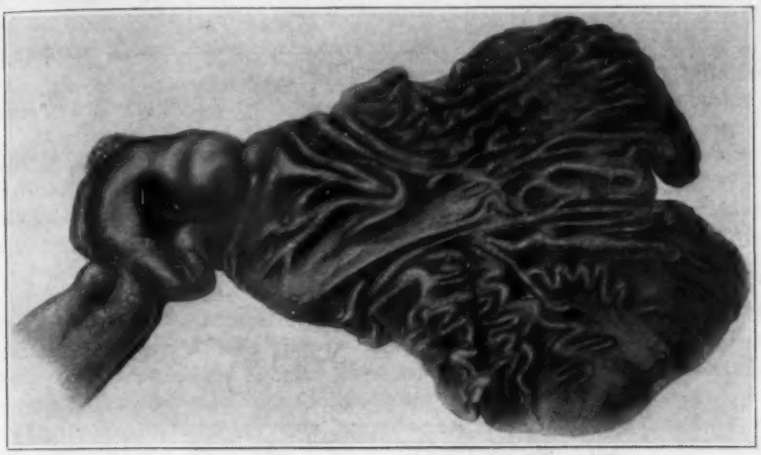

Fig. 6.—An anastomosis between the stomach and the jejunum, end-to-end with an Exalto short-circuiting operation (fig. 3). In this dog the ulcer occurred where there was still a little muscle left near the pyloric valve and penetrated into the jejunum which had been stripped of its muscle. This specimen shows the mechanical factor of the propelling peristaltic force of the stomach.

Fig. 7.—An end-to-end gastrojejunal anastomosis with an Exalto short-circuiting operation (fig. 3). The arrows point to the jejunum stripped of its muscle walls. A narrow superficial ulcer, covered by a diphtheritic membrane beginning exactly where the normal muscle layer starts its intact course, can be seen.

pouch, ulcers resulted in every animal operated on in this manner. We have used a technic described by Matthews and Dragstedt in several animals and in addition stripped the longitudinal and circular muscle layers of the ileum for a distance of 10 cm. distal to the anastomosis (fig. 4). Several animals were operated on

in this manner, but only six survived from eleven to one hundred and fifteen days. In none of the animals did an ulcer develop where the muscle was stripped. Dog 137 was found dead eleven days after the operation. The postmortem examination revealed two small superficial ulcerations in the ileum distal to the pouch where the longitudinal and circular muscle layers began their intact course. If we remember that Matthews and Dragstedt operated on six dogs in the same manner and found ulcers in each animal, our findings become interesting, since they compare well with the results of experiment type 1 recorded earlier, in which the muscle layers of the jejunum were stripped.

Type 3.—Again we wish to call attention to the fact that Winkelbauer operated on several dogs according to Exalto's short-circuiting technic, diverting the duodenal contents to the colon and excluding the motor part of the stomach, according to the method known in this country as that of Devine (fig. 2). Winkelbauer was able to observe ulcers in 100 per cent of these experiments. In twelve animals observed from nineteen to forty-three days, operated on by one of us (M. E. S.) according to the method described, large chronic ulcers formed in 75 per cent. These results were not as uniform as Winkelbauer's and can be explained by the fact that the alkaline duodenal contents were not diverted into the colon but somewhat higher into the small intestine. These twelve animals were used as control experiments. We then succeeded in keeping alive for from seventy-two to two hundred and twenty-five days four animals which were operated on in the manner already described. In addition, we performed an entero-anastomosis, according to the method of Finney, opposite the gastrojejunal anastomosis (fig. 2). Our object was to release the spasm of the jejunum at the gastro-anastomotic opening. None of these four dogs, observed for a long period of time, had ulcers. One of the control dogs operated on according to Exalto's short-circuiting method and Winkelbauer's and Devine's exclusion operation had a huge chronic, deep ulcer occupying the whole area of the jejunum anastomosed to the stomach. We formed an entero-anastomosis immediately distal to the ulcer. This dog was killed a month later; at that time we observed that the deep crater, measuring 3 cm., had filled in and was in the process of epithelization.

COMMENT

A brief summary of our data demonstrates that where the jejunum was anastomosed to the pyloric valve and the alkaline contents diverted away from the gastrojejunal anastomosis ulcers formed with regularity in each experiment. When the same procedure was used in ten dogs and three fourths of the circumference of the longitudinal and circular muscles was removed ulcers of the pylorus developed in only three animals. No ulcers were found in the part of the jejunum with the muscle layers denuded. In two dogs, in addition to the ulcer of the pylorus, there were definite ulcers exactly where the muscle began its intact course, or about 10 cm. from the pyloric valve. Again, in two other dogs no ulcers were found except where the normal muscle began its course, or about 10 cm. from the anastomosis of the pyloric valve. If one remembers that most of the experimental ulcers arise at the jejunum, separated from the pyloric valve by only 1 or 2 mm., this observation becomes most interesting (figs. 5 and 7).

In the second series of experiments we anastomosed the ileum to the Pavlov pouch according to the method of Matthews and Dragstedt [5] and stripped the muscle layers of the ileum for a distance of about 10 cm. (fig. 4). Ulcers developed in only one of six animals. This ulcer was found in a part of the ileum with its musculature intact distal to the part of the ileum denuded of its musculature. In view of the findings of Matthews and Dragstedt, the absence of ulcers in our experiments adds support to the observations already recorded.

Of four animals undergoing the Exalto short-circuiting operation, exclusion of a large distal part of the stomach and also an entero-anastomosis opposite the gastro-enterostomy, none had ulcers (fig. 2). Without an entero-anastomosis such a procedure produces ulcers in from 75 to 100 per cent of experiments. The number of animals in the last series is small but nevertheless suggestive, particularly if we consider that in the dog with the huge ulcer there were definite signs of healing following the entero-anastomosis near the ulcer. We have also observed that in most of our animals in which the longitudinal and circular muscles were removed in the jejunum or the ileum and subjected to the action of acid gastric juice the mucosa was pale in the area of the small intestine in which the muscle layers were stripped. Where the muscle layers were not stripped the mucosa was red and injected.

In recent publications Steinberg and Proffitt [6] and Steinberg [8] have reported numerous experiments in which it was demonstrated that the corrosive action of acid pepsin in the presence of certain mechanical factors produces peptic ulcers. It was pointed out that the muscular pyloric part of the stomach propelling the acid contents may be responsible for the actual localized trauma of the jejunum. An impediment in the form of a kink in the distal loop of the jejunum or a narrow gastro-intestinal opening favors the development of a jejunal ulcer. These procedures cause a delay in the emptying time and an increased acidity of the stomach contents. The ulcer found immediately in front of the kink would also demonstrate that there is a direct mechanical trauma determining the location of the ulcer. In the same publication Dr. Steinberg has mentioned the fact that the spastic conditions of the small intestine may be directly related to the etiologic factors in the experimental production of peptic ulcers. The predisposition of the subject, based on the neurogenetic theories which may influence the degree of psychic secretion, and the motility of the gastro-intestinal tract were also mentioned. It was pointed out how difficult it is to estimate the chemical and mechanical factors in some of the experiments.

In view of our findings in the present experimental work, how may we explain the absence of jejunal ulcer where the muscle layers are stripped?

Boldyreff [9] was the first investigator to point out that no matter how high the degree of acidity in the stomach is, the duodenum will not tolerate an acidity higher than 0.15 per cent. Burget and Steinberg,[10] Steinberg, Brougher and Vidgoff,[11] and, lately, Elman [12] have corroborated Boldyreff's work. Cannon [13] has observed that acidity on the duodenal side will close the pylorus. All these observations are important and suggest that when the acid is of a certain concentration the intestinal muscles contract and hold the acid until it is neutralized by some known or unknown factors. This speculation we are now following up by actual experimentation; we hope to report on it at a later date. The intestine with its muscle stripped is not able to contract. When acid of sufficent strength reaches the part of the intestine in which the muscle begins its intact course, a contraction takes place, and in a manner as yet not altogether explained a localized trauma takes place, producing an inflammation of the mucosa or an ulcer.

In our present experiments it would be impossible to imagine a propelling force producing ulcers where the muscle began its intact course, since this part of the intestine was separated from the pylorus by 10 cm. of jejunum with its muscle stripped and therefore lacking peristaltic activity. In one of our experiments two small chronic "kissing ulcers" occurred exactly as we see them in the duodenal cap. Perhaps the lumen contracted in such a manner that it exposed two small areas of the mucosa to the acid pepsin.

As already mentioned, when the muscle of the jejunum is intact most of the experimental ulcers are found immediately distal to the pylorus and separated from it only by a narrow strip of jejunal mucosa. This may be due to the fact that the part of the intestine which first receives the acid holds it in check until it is partially neutralized and therefore becomes harmless to the jejunal mucosa distal to the pylorus. This may also explain why we found ulcers only where the muscle began its normal course and not distal to this area. It must nevertheless

9. Boldyreff, W.: The Self-Regulation of the Acidity of the Gastric Juice, Quart. J. Exper. Physiol. **8**:1, 1915.

10. Burget, G. E., and Steinberg, M. E.: The Regurgitation of Intestinal Contents in Normal Dogs and Dogs with Posterior Gastro-Enterostomy, Am. J. Physiol. **60**:308 (April) 1922.

11. Steinberg, M. E.; Brougher, J. C., and Vidgoff, I. J.: Changes in the Chemistry of the Contents of the Stomach Following Gastric Operations, Arch. Surg. **15**:749 (Nov.) 1927.

12. Elman, Robert: Acidity in Duodenal Ulcer and Pyloric Obstruction, Surg., Gynec. & Obst. **49**:34, 1929.

13. Cannon, W. B.: The Mechanical Factors of Digestion, London, Edward Arnold & Co., 1911.

be mentioned that occasionally a few ulcers may be found a few centimeters away from the pylorus in the control experiments in which the muscle walls are left intact. It is possible that our findings may partially explain the fact that Dragstedt and Vaughn [14] were not able to produce ulcers in most of their experiments with parts of the intestine implanted in the stomach wall. Such a procedure would eliminate the ability of the implanted loops of the small intestine to contract and would produce a narrow lumen. Our observation does not exclude the possibility of the mechanical factors brought forward in a previous publication (Steinberg and Proffitt; [6] fig. 6).

In view of the theories of von Bergmann, Cushing and others concerning the neurogenic factors related to the gastroduodenal ulcers, our findings become most interesting and significant. At this time we are not ready to enlarge on all of the factors which may determine the formation of an ulcer. The sequence of hypermotility, spasm and degree of acidity are interrelated, and it is difficult to evaluate each factor separately. Matthews and Dragstedt [3] introduced a valve into the pylorus and were able to produce ulcers in four of eight transplants of intestine into the stomach. These investigators believed that it was the lack of regurgitation of the alkaline contents and therefore the heightened degree of acidity which were responsible for the formation of ulcers. On the other hand, it is our opinion that a valve fixed at a pyloric opening will also act as a foreign body, causing irritation and hypermotility. A valve 20 cc. below the gastrojejunal anastomosis would also be responsible for the irritability of the gastro-intestinal tract above this artificial impediment. We believe that the factor of the degree of acidity is of great importance, but we also believe that spasm and hypermotility are equally important.

SUMMARY AND CONCLUSIONS

Sixteen dogs operated on according to several technics which regularly produced ulcers failed to show evidence of ulcerations in the area of the jejunum, which was stripped of about three fourths of its longitudinal and circular muscle layers. In three dogs ulcers developed in the jejunum separated from the pylorus by about 1 or 2 mm. of normal jejunal mucosa. In five dogs ulcers were found in the jejunal mucosa distal to the area stripped of its muscle, exactly where the intact layers of muscle began their normal course, or about 10 cm. from the gastrojejunal anastomosis. The last observation according to our knowledge has never been made before.

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14. Dragstedt, L. R., and Vaughn, A. M.: Gastric Ulcer Studies; the Resistance of Various Tissues to Gastric Digestion, Arch. Surg. **8**:791 (May) 1924.

In four dogs with a large exclusion operation according to Devine and an Exalto short-circuiting operation, which regularly produce ulcers, ulcers did not develop when an entero-anastomosis was made opposite the gastro-enterostomy.

The modus operandi in our experiments which prevented ulcerations appears to be the release of spasm through the stripping of the jejunal muscle wall or through an additional entero-anastomosis opposite the gastro-anastomosis. Since in most of the experiments of the present series with the muscle layers stripped there was no vis à tergo, we believe that a certain degree of acidity depending on the particular area of the intestine causes it to contract until the degree of acidity is reduced to a certain strength. A prolonged contact of unneutralized pepsin with intestinal mucosa causes an ulcer, provided there is also present the possibility of the narrowing of the lumen through spasm. This, however, does not exclude some of the other mechanical factors elaborated by one of us (M. E. S.).

Our observations support the neurogenic theory as an important factor in the etiology of ulcerations of the upper gastro-intestinal tract.

MALIGNANT LYMPHOMA OF THE GASTRO-INTESTINAL TRACT

A. C. PATTISON, M.D.
IOWA CITY

Malignant lymphoma is a neoplasm that arises from the lymphatic tissues and is due to a proliferation of atypical cells of the lymphatic series. They extend not only locally and regionally, but often eventually to distant organs. Frequently they assume the forms of diffuse infiltrations, and some authors believe that in such cases a continuous lymphatic connection, including a retrograde process, can be demonstrated between the primary and secondary growths. Other forms are diffuse at the onset, and a definitely localized primary focus cannot be ascertained. Changes in the circulating blood stream are either absent or of no differentiating value, with the exception of a terminal leukemia seen in some cases.

The lesions have been extensively classified, but recently there has been a tendency among pathologists to consider these various conditions as different manifestations of the same pathologic process. Thus, the term malignant lymphoma has come into use.

There is one manifestation of the disease which is of special interest to the surgeon, and that is the group in which the primary nidus is well localized and metastases are only local or regional, though terminally more distant extensions are occasionally seen. This type of malignant lymphoma is usually placed in the lymphosarcoma group. Since 1930, six such cases, all with localization in the gastro-intestinal tract, have come to operation in the surgical service at the University Hospital. A report of the six cases is the object of this paper.

As will be noted in the reports, symptomatically the lesions are not characteristic, and a correct preoperative diagnosis was not made in any case. In cases previously reported in the literature, the age of the patients varied from 3½ to 85 years. As a rule the average age incidence is from fifteen to twenty years below that of carcinoma of the gastro-intestinal tract. However, because of the wide variance of age in both types of lesions, this point is of little value in arriving at a differential diagnosis.

Pathologically, lymphomas differ from carcinoma in that they arise in the submucosa and infiltrate the submucosa and muscularis. Ulceration, though not infrequent, is often absent, and when it occurs, is due to necrosis from pressure and loss of blood supply rather than to neoplastic invasion.

From the Department of Surgery, University Hospital.

In the stomach, the lesions when first seen vary from a small, well localized nodule to a diffuse infiltration of practically the entire wall of the stomach. The wall may simply be thickened, which is the usual condition, or sessile and polypoid masses may obtain. Frequently, the tumors are situated in the antrum, but usually far enough from the pylorus that obstruction by tumor is uncommon. The cardia is rarely involved except in the diffuse lesions. The lesion most commonly occurs on the lesser curvature. Secondary lesions are common, and usually occcur in the form of local involvement of the regional lymph nodes. Extension to the liver is unusual.

In the small intestine, the lower part of the ileum is most commonly involved, though lesions have been reported to occur in any part of the small intestine from the duodenum to the terminal portion of the ileum. The lesion may be diffuse, nodular, sessile or polypoid. The tumor, arising in the submucosa, early extends through and destroys the muscularis. Metastasis to the regional lymph nodes occurs early. Aneurysmal dilatation of the intestine at the site of the neoplastic invasion is frequent. This is due to destruction of the muscle fibers with resulting separation or to involvement of the submucosa, with subsequent effect on its plexus of nerves. Obstruction is not frequent. When it occurs, it is usually late in the disease and is due to pressure from the enlarged mesenteric glands or as a result of fibrosis, which may occur late in the disease. DeNoyelles [1] reported a case of a polypoid malignant lymphoma protruding into the lumen and resulting in obstruction. Partial obstruction occasionally occurs when a large segment is involved as a result of loss of peristalsis. Intussusception is fairly frequent, the tumor occupying the apex of the invaginated loop.

In the large intestine, the lesions are similar to those in the small intestine, though the lumen is not often encroached on. The most common site of occurrence in this section is at the cecum, though lesions may also occur in any portion of the large intestine. One in this series was mistaken for carcinoma of the rectum.

Results of the laboratory examinations are in no way distinctive. The roentgen-ray diagnosis following ingestion of a barium sulphate mixture is usually carcinoma, though a diagnosis of gastric ulcer is sometimes made. In a fair number of cases the examination reveals no abnormality. In the earliest stage, that is, when the submucosa alone is involved, the lesion does not interfere with the muscular function of the stomach. Ulceration of the mucosa is not an early pathologic change. Holmes, Dresser and Camp,[2] reporting eight cases studied roentgenologically, stated that they diagnosed only one case preoperatively, and in that there was peripheral involvement of lymph nodes, and one

1. DeNoyelles, P. L.: Lymphosarcoma of the Intestine, Ann. Surg. **76**:229, 1922.

2. Holmes, G. W.; Dresser, Richard, and Camp, J. D.: Lymphoblastoma, Radiology **7**:44, 1926.

of the nodes was taken for biopsy. Two of their cases showed a normal roentgenologic appearance. Observations on the remaining six were: sluggish, irregular peristalsis which did not pass over the site of the lesion; a filling defect, usually annular, and gastric stasis. In brief, the roentgenologic appearance does not differ from carcinoma, except in some cases in which peristalsis is not interfered with to the extent usually seen in carcinoma of the stomach. Roentgen examination is of little value in the diagnosis of most lesions involving the small intestine, the patency of the intestine and the lack of early ulceration militating against a diagnosis. It has been suggested that an examination every one or two hours after the ingestion of a barium sulphate meal may aid by determining a temporary retardation of the flow of barium.

REPORT OF CASES

The patients in the following six cases were operated on in University Hospital.

CASE 1.—*History.*—R. I., a woman, aged 58, was first seen in the medical service of the University Hospital complaining of gas and heaviness in the stomach. Nine months before admission she noticed that she was becoming pale. There had been a gradual loss of weight in the preceding two months, from 98 to 90 pounds (44 to 40 Kg.), with considerable loss of strength. There was no history of hematemesis or melena.

Physical examination revealed a thin, undernourished, asthenic woman. The heart and lungs were not remarkable. The blood pressure in millimeters of mercury was 130 systolic and 75 diastolic. The spleen was palpable. There was a rather indefinite abdominal mass, not tender, just above and to the left of the umbilicus.

On laboratory examination the urine showed a trace of albumin. The blood count showed: red cells, 4,000,000 per cubic millimeter; white cells, 7,100, and hemoglobin, 65 per cent. The differential count was essentially normal. A fractional gastric analysis revealed no free acid until histamine was given, when it reached 10. The Wassermann reaction was negative. Visualization of the stomach by means of a barium meal revealed evidence of a filling defect within the lumen of the stomach in the region of the pars pylorus which had a more or less loculated appearance, and suggested the presence of multiple polypi.

A tentative diagnosis of gastric polyposis was made, and after suitable preoperative preparation an exploratory operation was performed on March 30. In the prepyloric end of the stomach was a mass about the size of a lemon. It was elastic and spongy, and could be moved through a fairly wide excursion, though it did not extend down to the pyloric ring. There was no evident pathologic change in the wall of the stomach. There were many lymph nodes in the greater and lesser omenta, the largest being the size of a hickory nut. Two were removed for microscopic study. The lower end of the stomach was then resected, a Billroth I technic being used. The patient left the operating table in good condition. Soon, however, she began to raise small amounts of blood. This was not controlled by giving blood in the buttock. A transfusion was given, but she did not rally, and died on April 1. Permission for a postmortem examination was not obtained.

Fig. 1 (case 1).—The loculated filling defect in the pars pylorus after the ingestion of barium. The stomach was entirely empty in six hours.

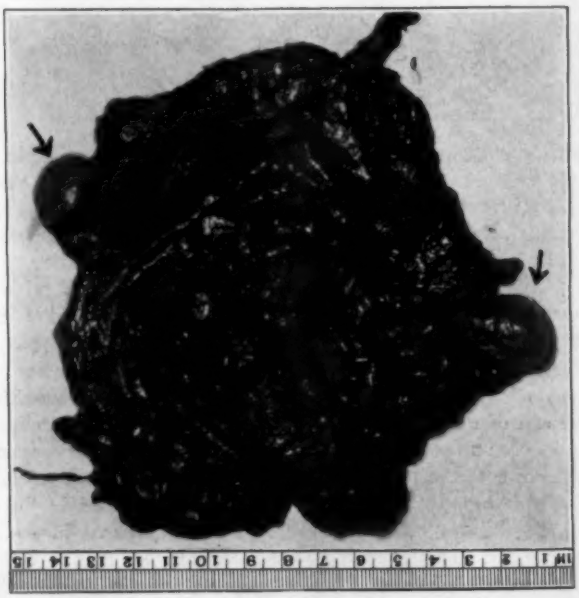

Fig. 2 (case 1).—The resected portion of stomach. The arrows point to two sectioned lymph nodes.

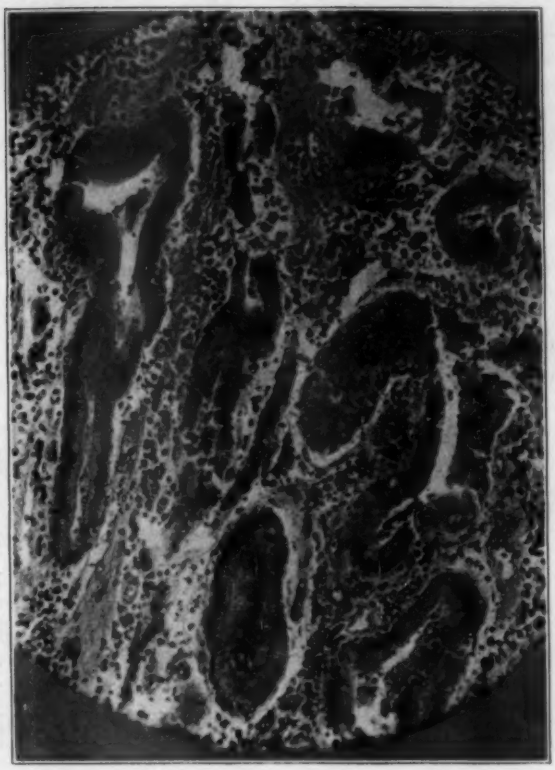

Fig. 3 (case 1).—A section from the polypoid mass showing the numerous alveoli and tubules in the adenoma. Many inflammatory cells are present in the supporting connective tissue.

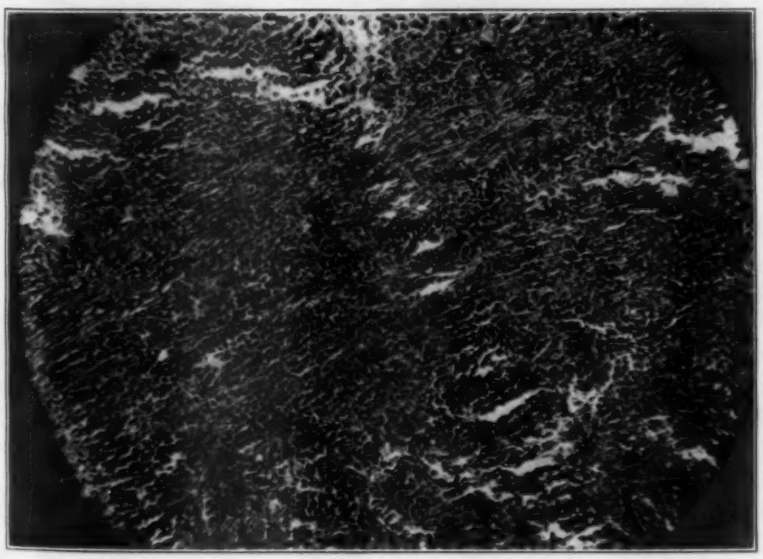

Fig. 4 (case 1).—In the wall beneath the adenoma are the invading neoplastic cells which are uniform and of the plasma cell type. Invasion into the muscular layer, with separation of the fibers, is a prominent feature.

Microscopically the polypoid mass revealed numerous alveoli and tubules embedded in a loose, vascular fibrous connective tissue. In the surrounding connective tissue were many plasma cells and some lymphocytes and eosinophils. A section through the wall of the stomach at the base of the mass showed marked infiltration of plasma cells, so great that in some places the structure of the wall was obliterated. Sections of the lymph nodes showed replacement of the normal architecture by plasma cells and a few small lymphocytes and endothelial cells. The diagnosis was adenoma of the stomach and malignant lymphoma of the stomach, with metastases to the regional lymph nodes.

Case 2.—G. M., a man, aged 20, was first admitted to the medical service of the University Hospital complaining of pain in the upper part of the abdomen,

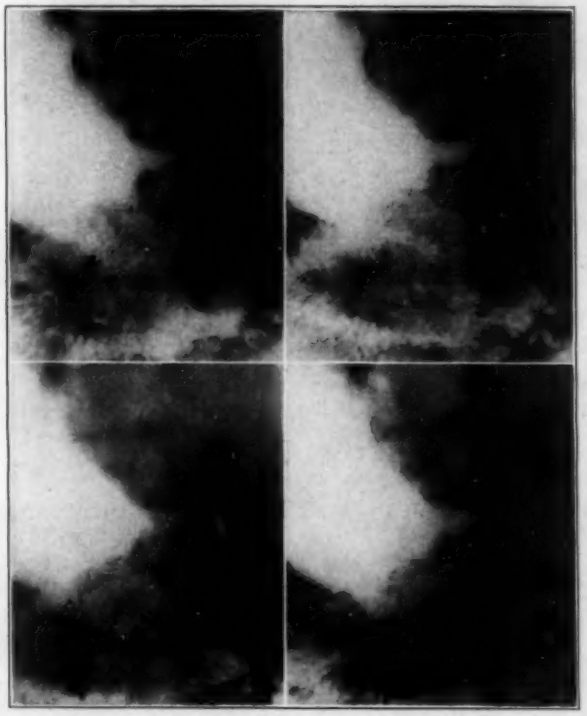

Fig. 5 (case 2).—Following ingestion of a barium mixture this film, taken postoperatively, shows the functioning gastrojejunostomy stoma and a persistent defect in the region of the pylorus.

vomiting and loss of weight. The abdominal pain began about one year before admission as a dull discomfort, present most of the time, but increased by eating. There had also been frequent vomiting after eating and a loss of 20 pounds (9 Kg.). One year before admission, there was an injury with possible fracture of a vertebra and loss of sensation in the legs for forty-eight hours.

Physical examination in the medical service and later in the surgical service revealed nothing relevant except tenderness over the first lumbar vertebra and slight rigidity and tenderness in the epigastrium.

Laboratory examination revealed: red blood cell count, 4,900,000 per cubic millimeter; white blood cell count, 7,600, and hemoglobin, 85 per cent. The

differential blood count was normal. Urinalysis gave negative results. A fractional gastric analysis revealed a slight hypo-acidity, the high level of free acid being 15 and the high level of total acid being 30. Examinations of stools revealed a positive Meyer reaction on two occasions. Visualization of the stomach by means of a barium meal revealed a persistent niche on the greater curvature in the pyloric region, suggesting a penetrating type of ulcer. Films of the chest, spine and colon were essentially normal.

A positive diagnosis could not be made, the two major probabilities being carcinoma of the stomach and gastric ulcer. It was decided to place the patient on an ulcer regimen for one month, and if no improvement occurred to perform an exploratory operation. This was done, the patient receiving no relief from his symptoms.

Fig. 6 (case 2).—Infiltration of the submucosa with neoplastic cells and the displacement of the gastric glands were prominent features. Note that the gastric mucosa in this section is intact. The type cell of the neoplasm is the lymphocyte.

At operation, on November 30, no lesion was found at first in the pyloric region to account for the roentgen-ray findings. However, the entire wall of the stomach was thickened and less elastic than normal. Along the greater curvature of the stomach several enlarged lymph nodes, one the size of a hazelnut, were found in the mesentery. It was felt that visualization of the inside of the stomach was necessary to arrive at a conclusion, so a 2 inch (5 cm.) incision was made longitudinally near the pylorus on the anterior wall. Both muscular and submucosal layers were definitely thickened and inelastic, and a sensation of friability was obtained. There were several large, irregular areas where the mucosa seemed to be lost or superficially ulcerated. In one or two areas there was heaping up of mucosa. The roentgen-ray findings were explained on viewing the interior of the stomach. A small pouching had taken place at the site of the niche. This was due to the fact that a small area of the wall of the stomach was less involved than

the area surrounding it. A portion of the wall of the stomach was removed for biopsy, the incision closed and a posterior gastro-enterostomy done.

Microscopic examination of the biopsy specimen revealed areas of ulceration of the mucosa. The submucosa was packed with cells of the lymphatic series, both adult and blast cells being noted. Mitotic figures were numerous. There was little stroma present. The gastric glands were practically completely replaced by the lymphatic cells, but the tissue seemed fairly well limited to the submucosa, the muscle layer showing only a slight lymphocytic infiltration. Sections of the lymph nodes showed chronic lymphadenitis. The pathologic diagnosis was malignant lymphoma of the stomach.

The postoperative course was essentially uneventful. After receiving the pathologic report, a course of irradiation therapy was given, and the patient was discharged. He was seen again, three months after operation, at which time he felt much better, though he had vomited on several occasions. He had gained 20 pounds. Visualization of the stomach by means of a barium meal showed an increase in the size of the filling defect. The gastro-enterostomy stoma was functioning well. He was given a course of irradiation therapy. He next returned eight months after the operation. At that time there were no gastro-intestinal symptoms, and the patient was doing manual labor. Visualization of the stomach by means of a barium meal showed some regression in the size of the filling defect and a functioning gastro-enterostomy stoma. He was again given a course of irradiation therapy. He was last seen fifteen months after the operation, at which time he was in the best of health and had no complaints. The condition of the stomach, however, remained unchanged. He was given another course of irradiation therapy at that time.

Case 3.—L. S., aged 4, was admitted to the surgical service of the University Hospital on March 10, 1932, with a history of severe pain in the midepigastrium beginning on Oct. 13, 1931, which was accompanied by nausea and vomiting. On October 15 he vomited continuously for two hours. He was given tincture of belladonna, with relief. Since then he had had frequent attacks of vomiting and cramplike pain in the upper portion of the abdomen, and at the time of admission the pain was nearly continuous.

Physical examination revealed a fairly well developed and well nourished Mexican boy. The tonsils were moderately enlarged. There was a rachitic rosary. The abdomen was slightly distended. A mass about 10 cm. in length could be palpated, lying transversely in the abdomen at the level of the umbilicus. There was slightly diffuse abdominal tenderness.

Laboratory examination revealed: red blood cell count, 4,600,000 per cubic millimeter; white blood cell count, 10,000; hemoglobin, 80 per cent and differential count, normal. Urinalysis gave negative results. Visualization of the large intestine by means of a barium enema and a six hour examination after the ingestion of a barium meal revealed evidence of an intussusception extending nearly to the splenic flexure of the large intestine.

He was operated on on March 11. An intussusception involving the large intestine and terminal portion of the ileum and extending as far as the splenic flexure was found. The intussusception was reduced with ease. After reduction, a striking change remained at the ileocecal junction. Involving the wall of the terminal portion of the ileum was a band of firm, inelastic grayish-white tissue, about 1 inch (2.5 cm.) wide. This segment of the intestine was several times thicker than the wall proximal to it. The thickening extended onto the wall of the cecum toward the base of the appendix. In the terminal 3 inches (7.6 cm.)

Fig. 7 (case 3).—A barium mixture was injected into the large intestine. This film reveals what was thought to be localized areas of spasm, but it was an intussusception.

Fig. 8 (case 3).—This film, taken twenty-four hours following the ingestion of a barium mixture, is typical of intussusception into the large intestine.

Fig. 9 (case 3).—The cellularity is well illustrated. Little stroma can be seen. The mucosa is ulcerated, but is intact in other areas.

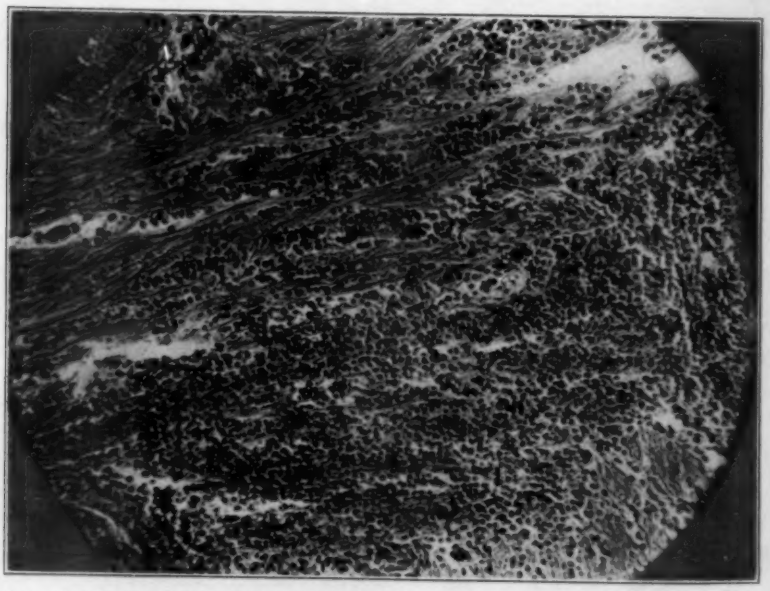

Fig. 10 (case 3).—The muscularis of the ileum is being invaded by the neoplasm, with a separation of the fibers. The resulting loss of tone is a factor in the local dilatation of the intestine.

of ileum, what was thought to be a mass was felt in the lumen. A resection of 5 inches (12.7 cm.) of cecum and 4 inches (10.1 cm.) of the terminal portion of the ileum was done, and a lateral anastomosis made.

On opening the ileum the portion thought to have been a mass was found to be made up of nodular areas of thickening of the submucosa. Areas of ulceration were present. In the region of the band, the whole wall was firm, inelastic, grayish white and very cellular. Microscopically, the mucosa was ulcerated for the most part. Cells of the lymphocytic series formed the base of the ulcer and extended down into and through the muscular layer to the serosa. Mitotic figures were numerous. The cells were packed close together, and laid in a thin connective tissue stroma. The pathologic diagnosis was malignant lymphoma of the ileum and ileocecal junction.

The boy had a fairly uneventful postoperative course, and was discharged on April 1. Although we requested his return he did not come back to the hospital. A letter from his father on July 10, 1933, informed us that the boy was in excellent health and in no way appeared to be ill.

Case 4.—J. C., a man, aged 23, had been admitted to the University Hospital four times previously to his admission on June 26, 1931, for control of diabetes mellitus and removal of bilateral cataracts. He was admitted to the genitourinary service complaining of a mass in the right side of the abdomen, first noticed in February 1931. At the time the mass was first noticed he was constipated. There was no pain, but the tumor was somewhat tender. In March 1931, following his evening meal, he became nauseated, and diarrhea developed which lasted for twenty-four hours. He had twelve watery stools. He had no further discomfort following this episode, but he noticed that the mass became tender when he was constipated. A cystoscopic examination revealed the mass to be intraperitoneal, and it was thought to be in the hepatic flexure of the colon. He was then transferred to the surgical service.

Physical examination revealed a well developed and well nourished white man. There was mild pyorrhea alveolaris. Both pupils were irregular and fixed in places, and both corneas were scarred. A mass, firm and freely movable, was found in the right side of the abdomen. The lower margin was about two fingerbreaths above the crest of the ilium. It was somewhat egg-shaped, and could barely be felt posteriorly. On deep inspiration it moved 4 cm. downward. It was slightly movable in lateral and mesial directions. Fluid was demonstrable in the peritoneal cavity.

Laboratory examination revealed: red blood cell count, 5,200,000 per cubic millimeter; white blood cell count, 6,800, and hemoglobin, 80 per cent. Urinalysis and the Wassermann test gave negative results. Visualization of the large intestine by means of a barium enema revealed a marked irregularity and spasticity involving the ascending colon.

He was placed on diabetic management, and an exploratory laparotomy was performed on July 3. A moderate amount of clear straw-colored fluid was found in the peritoneal cavity. In the region of the cecum a mass the size of a large orange was encountered. This involved the terminal portion of the ileum for 3 inches, as well as the cecum. The wall was thickened and somewhat reddish. The mass involved the serosa of the cecum over one area the size of a silver quarter. Here the wall was firm and inelastic. There was some infiltration into the mesentery, but no involved lymph nodes were encountered. The lesion resembled chronic hyperplastic tuberculosis. A resection of the terminal ileum and

large intestine, up to the proximal 4 inches of the transverse colon, was performed and a lateral anastomosis made.

On making an opening into the cecum, the mass was found to arise from the submucosa. The mucosa was ulcerated in certain areas. The muscularis was infiltrated, and the cut section of the tumor was grayish white and cellular. Some enlarged glands were found in the mesentery. Microscopically, the tumor consisted of lymphoblasts packed closely together. Many mitotic figures were present. The stroma was scant. In one area, the neoplasm extended through the muscularis to the serosa. The mesenteric lymph nodes showed a similar replacement. The pathologic diagnosis was malignant lymphoma of the cecum, with metastases to the mesenteric lymph nodes.

The postoperative course was complicated by cellulitis of the scrotum which extended up over the abdomen onto the chest wall. On July 23 the cellulitis was

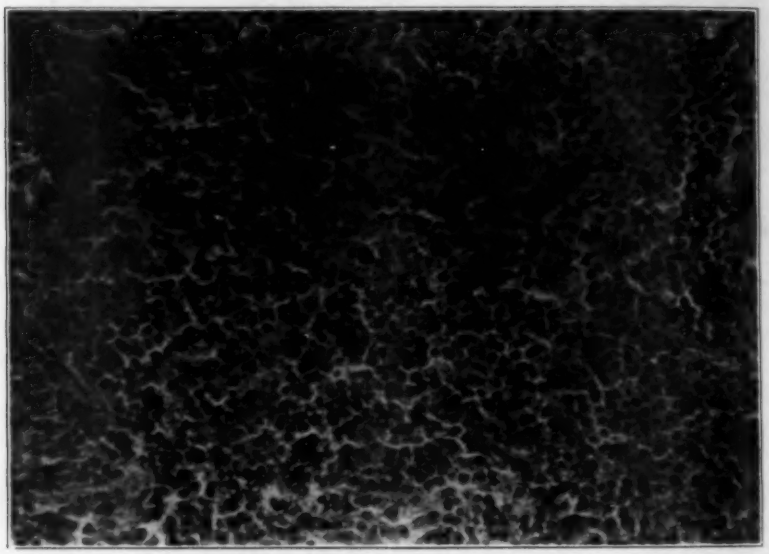

Fig. 11 (case 4).—High power photomicrograph showing the cellularity of the neoplasm. Only a small amount of reticulum is present. Numerous mitotic figures are present.

apparently controlled. However, on July 27, spontaneous hypoglycemia developed which did not respond to therapy, and the patient died. Permission for a post-mortem examination was not obtained.

Case 5.—B. R., a woman, aged 42, was admitted to the surgical service of the University Hospital on June 19, 1932. For six months she had noticed an increasing weakness, and had lost 20 pounds. Two months before admission she was seized by a severe cramping pain, beginning just to the right of the umbilicus and radiating down to the symphysis and up beneath the right costal margin. Since then, she had similar attacks every three or four days. Residual tenderness was always noticed in the right upper quadrant of the abdomen. For six weeks before admission she had also had several attacks of dull pain in the right upper quadrant which would radiate around to the back. She was occasionally nauseated, but never vomited. There was no jaundice or bloody stools.

Physical examination revealed a well developed but emaciated white woman. There was slight enlargement of the right lobe of the thyroid gland. There was moderate spasticity of the entire right side of the abdomen. A palpable and freely

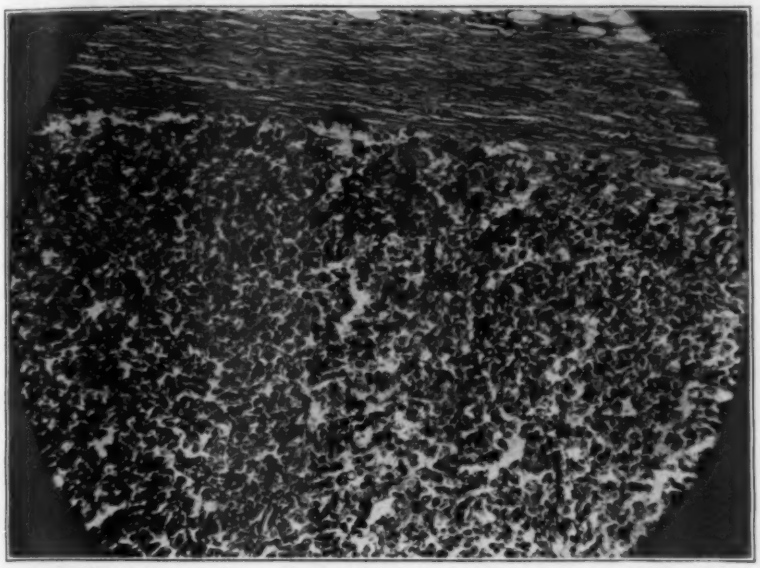

Fig. 12 (case 5).—The structure of the lymph node has been replaced by neoplastic tissue.

Fig. 13 (case 5).—Photomicrograph showing extension in the submucosa. The mucosa is intact for a considerable distance over the tumor.

movable mass was present in the right lower quadrant, which was slightly tender. There was slight tenderness in the region of the gallbladder.

Laboratory examination revealed: red blood cell count, 3,100,000 per cubic millimeter; white blood cell count, 6,700, and hemoglobin, 60 per cent. The

Wassermann reaction was negative. Visualization of the large intestine by means of a barium enema revealed a redundant ptotic colon. A cholecystogram revealed a nonvisualizing gallbladder.

An exploratory laparotomy was performed on June 27. All the abdominal organs lay unusually low. The cecum was delivered through the incision. In its mesentery was a mass about the size of a tennis ball, which was made up of enlarged lymph nodes. An intussusception of the distal ileum into the cecum was noted, and in the lumen of the cecum could be felt a mass, roughly globular, but irregular in contour and about 2 inches in diameter. A resection of the terminal portion of the ileum, cecum and ascending colon was done, and a lateral anastomosis made. All lymph nodes were thought to have been removed. There were some adhesions around the gallbladder, but when these were separated the gallbladder appeared to be normal.

When the cecum was opened, the mucosa over the palpable mass was not ulcerated. On cut section it was grayish white and homogeneous. The mass seemed to arise from the submucosa, and did not appear to invade the muscularis. Microscopically, the neoplasm consisted of a compact, structureless, cellular neoplasm which involved the submucosa and invaded the muscularis. The cells were lymphocytes, and many mitoses were present. The lymph nodes showed a similar histologic picture. The pathologic diagnosis was malignant lymphoma of the cecum, with metastases to the mesenteric glands.

The postoperative course of the patient was uneventful. She was not seen again until fifteen months after operation. At that time she presented no complaints and no evidence of a recurrence. Visualization of the stomach by means of a barium meal and visualization of the large intestine by means of a barium enema revealed essentially normal organs. The anastomosis was functioning well.

The patient recently returned to the hospital (Sept. 15, 1934) in a much debilitated condition and with palpable intra-abdominal masses.

Case 6.—E. E., a woman, aged 70, was admitted to the surgical service of the University Hospital on Dec. 29, 1932, complaining of pain in the rectum and bloody stools. She had always been well until April 1932, when she passed some bright red blood by the anus. This happened again the following July. Three months previous to admission she began to have pain with the passing of stools. There had been no change in the character of the stools. She had had hemorrhoids for a number of years. For the past year she had had a dull aching pain in the lower part of the back. She had lost 20 pounds in the previous year. There was a history of carcinoma of the stomach in the patient's mother and carcinoma of a breast in one of the patient's sisters.

Physical examination revealed a fairly well developed and well nourished white woman, who was not acutely ill. There was bilateral middle ear deafness. There was a cauliflower-like mass about the size of a small fist in the rectum on the right. This was freely movable.

Laboratory examination revealed: red blood cell count, 3,950,000 per cubic millimeter; white blood cell count, 9,500 and hemoglobin, 60 per cent. Urinalysis and the Wassermann test gave negative results.

A diagnosis of carcinoma of the rectum was made. On December 31, an exploratory operation was performed through a left lower transrectus incision. The lesion did not extend above the pelvic floor, and no evidence of metastases was found, so a loop of the sigmoid flexure was brought out through the incision, the loop subsequently being opened on Jan. 9, 1933. On January 24, she was again operated on, a perineal resection of the distal sigmoid flexure and rectum being done. No evidence of invasion into the surrounding tissues was noted. Following

Fig. 14 (case 6).—The edge of the tumor of the rectum. The cells have invaded through the muscularis.

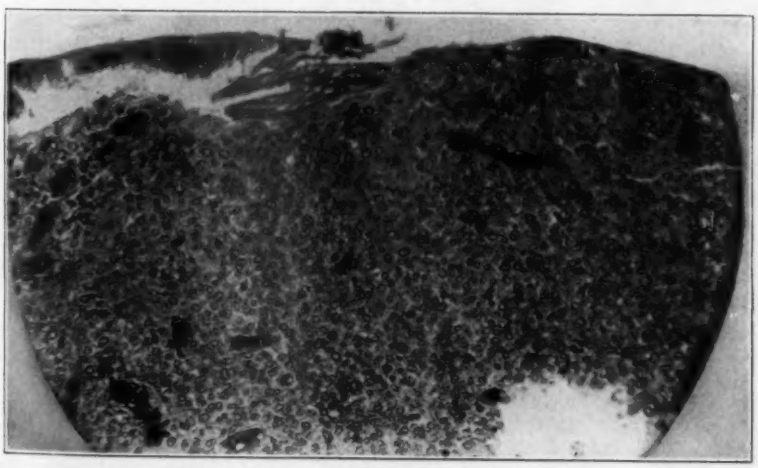

Fig. 15 (case 6).—The edge of the ulcerated mucosa shown in figure 14. Many mitotic figures are present in the bulk of the tumor.

this procedure, the patient progressed satisfactorily, except that there was a profuse and foul discharge for a number of days. She was discharged from the hospital on February 15, with only a small amount of purulent discharge coming from the wound. She did not receive roentgen-ray therapy.

On pathologic examination the mass did not present the cauliflower-like appearance noted on physical examination. This may have resulted from a regression of the tumor following colostomy. The mucosa was ulcerated over the central portion of the mass. On cut section the tumor was grayish white and granular, and apparently invaded through the muscularis. There were numerous lymph nodes in the surrounding fat which appeared to be normal. Microscopically, the mucosa extended up part way along the neoplasm, and gradually faded out into the tumor tissue. The majority of the cells were round cells of moderate size, with an oval, violet-staining nucleus and a pale pink cytoplasm. The cells showed many mitoses. Scattered among them were lymphocytes and many plasma cells. A few eosinophils were present. The tumor had invaded the outer muscular coat. The lymph nodes showed no evidence of neoplasm. The pathologic diagnosis was malignant lymphoma of the rectum.

The patient has not returned to the hospital since the operation. However, a recent letter from her nurse stated that the perineal wound is still draining, the patient is rapidly losing weight and strength and is bedfast.

SPASM OF THE ORBICULARIS OCULI IN LOCAL TETANUS

K. P. A. TAYLOR, M.D.
HAVANA, CUBA

The ordinary development of tetanus in man comprises tonic spasm of the masseter muscles (trismus) with spreading to other groups of muscles (descending tetanus). Occasionally the spasm is initiated in the wounded limb and extends to the whole body (ascending tetanus) or remains localized in the affected member (local tetanus). Spasm or paralysis limited to one or more muscles of the head may be considered a variety of local tetanus.[1]

In reviewing reported cases of local tetanus placed on record prior to the World War and occurring in civil practice, I [2] encountered only four cases, of which I was doubtful;[3] to this number I added a civil case of the monoplegic type developing in a patient who had not received prophylactic antitoxin. During the war the number of cases of local tetanus occurring in inoculated patients rapidly increased, causing an interest among French investigators reflected in the monograph by Courtois and Suffit-Giroux on abnormal forms of the disease. The comparative frequency of local tetanus in military practice was ascribed by Etienne [4] to the neutralization of toxin circulating in the blood stream by the prophylactic injection, with prevention of general manifestations. Francaise [5] believed that the prophylactic injection was not always effective in forestalling the development of local tetanus, since it could not affect the toxin already combined with tissues of the nervous system. Chauvin [6] also subscribed to these views. In the succeeding years of

1. Rabinovich, G. B.: Experimental Study of Local Tetanus and Its Special Form of Paralytic Head Tetanus, Klin. med. **10**:213, 1932.

2. Müller, G. P., and Taylor, K. P. A.: Local Tetanus, Ann. Surg. **74**:110 (July) 1921.

3. Axhausen, L.: Ueber lokalen Tetanus beim Menschen, Deutsche Ztschr. f. Chir. **78**:265, 1905. Demontmerot, M.: De la forme paraplégique dans le tetanos chronique, Thèse de Paris, 1904. Von Esau, F.: Ein Fall von lokalem Tetanus der Hand, Deutsche med. Wchnschr. **36**:706, 1910. Jacobsen, N., and Pease, H. D.: The Serum Therapy of Tetanus, Ann. Surg. **44**:321 (Sept.) 1926.

4. Etienne, G.: Tetanos partiels essentiels, Paris méd. **29**:91, 1918.

5. Francaise, H.: Tetanos localizé, Paris méd. **29**:255, 1918.

6. Chauvin, E.: Les tétanos localisés des membres, Presse méd. **26**:295 (June 10) 1918.

the war, the ratio of cases of local tetanus to those of general tetanus became progressively higher. Bruce [7] attributed this increase to the more widespread use of the prophylactic injection and to more frequent recognition of mild and obscure cases.

Ashurst [8] pointed out the similarity between local tetanus and the "experimental" tetanus which had long been observed to follow the injection of relatively nonvirulent organisms into the limbs of animals. He attributed local tetanus to an ascent of toxin to the spinal cord, creating an arc of lowered threshold in the affected area. The toxins of more virulent infections were thought to be conveyed to the cord by the blood, affecting the shorter nerves supplying the muscles of mastication, the neck and the back. I assume that local tetanus developing after the prophylactic injection of antitoxin is the residuum of what would have been a virulent generalized infection had the preventive dose not been given. On the other hand, local tetanus occurring without prophylactic injection is probably the counterpart of the usually mild "experimental" tetanus. The following case and the previous case reported by me occurred in nonimmunized persons.

REPORT OF A CASE

T. S., a white sailor, aged 42, was admitted to the Anglo-American Hospital in Havana on Oct. 20, 1932. He complained of spasm of the right eye and difficulty in separating his teeth. Seventeen days before, he had cut his scalp against sea bottom while diving in the harbor at Kingston, Jamaica. The laceration had been sutured, but medical attention had not been sought since the day of the injury. Ten days later partial closure of the right eye was noted; this was followed by stiffness of the masseter muscles. On examination it was observed that the right palpebral fissure was narrowed by a spastic contraction which could not be relaxed and that the right corner of the mouth was slightly elevated. The incisor teeth could be separated about ¼ inch (0.64 cm.). In the right frontal region was an encrusted, infected scalp wound, 8 cm. long, apparently healed by serum oozing from its lower end. The sutures were removed and a wet dressing applied. The temperature was 99 F. The tendon reflexes were not exaggerated, nor were there other significant physical findings or data from the history. There was no evidence of a present or preceding cellulitis of the scalp or forehead.

A presumptive diagnosis of local tetanus was made, and 5,000 units of antitoxin was administered intraspinally and 10,000 units intramuscularly. Both doses were repeated on the following day, and thereafter 5,000 units was given intramuscularly every six hours. The spinal fluid was normal cytologically and serologically. The roentgen appearance of the cranium was normal.

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7. Bruce, D.: Analysis of One Thousand Four Hundred and Fifty-Eight Cases of Tetanus, J. Hyg. **19**:1 (July) 1920.

8. Ashurst, A. P. C.: Report on Tetanus, Arch. Surg. **1**:407 (Nov.) 1920.

The patient's general and local condition remained unchanged. The wound on the scalp appeared to be uniformly healed. Because of the failure of the facial spasm and trismus to respond to treatment it was believed that the wound harbored tetanus bacilli. Accordingly on October 24 the wound was incised under local anesthesia. Beneath the pericranium of its anterior margin a collection of thin pus was encountered. The entire wound was swabbed with phenol, lightly packed and left open. Unfortunately no culture was made.

On October 28, both the facial spasm and the trismus were virtually abolished, the patient being able to open the affected eye widely (fig. 1 *B*). The dose of antitoxin was reduced to 10,000 units daily, and on November 1, its administration was discontinued and the patient discharged in satisfactory condition, with the wound on the scalp healing by second intention.

Fig. 1.— *A*, spasm of right orbicularis oculi seven days after onset, before the beginning of treatment. *B*, ability to relax orbicularis after completion of antitetanic serum therapy.

TREATMENT

In this instance, 10,000 units of antitoxin was given intrathecally and 180,000 units intramuscularly. It is probable that similar results could have been secured by the administration of a smaller quantity of antitoxin. However, the uncertain prognosis of cephalic tetanus indicated the large dosage. It is doubtful that cure would have resulted had the site of infection not been surgically exposed and phenolized; this fact emphasizes the value of phenol as originally stressed by Bacelli and recently by Bates.[9] The latter believed that 7,500 units intraspinally and a total of 40,000 units intramuscularly, given on the day of diagnosis, would suffice as well as larger doses. The problem of dosage remains unsettled, many observers believing that in severe cases of generalized tetanus cure has been effected by heroic doses (a total of

9. Bates, C. O.: Treatment of Traumatic Tetanus, Am. J. Surg. **18**:58, 1932.

200,000 or more units). Not even these large quantities can be depended on to arrest the disease in all cases. Slimon,[10] for example, reported a case of cephalic tetanus with facial paralysis in which treatment was started on the day of initial symptoms. A total of 300,000 units was administered intravenously and intraspinally before a fatal outcome on the eighth day. In Grant's [11] case 160,000 units was employed, with recovery, in a patient aged 7 years.

INCIDENCE OF LOCAL TETANUS

In contrast to four cases reported before the World War, I have assembled reports of sixty-two cases recorded since 1921. Seventeen of these involved an extremity and forty-five, the head. An analysis of these cases is not attempted (see bibliography).

In general it may be said: that local tetanus is not exceedingly uncommon in civil practice; that it occurs with or without prophylactic inoculation, and that in peripheral cases the prognosis is fair, and in the cephalic type, guarded. In diagnosis, hysterical contractions and paralysis due to injury of cranial or peripheral nerves present the main difficulties. The case reported here showed tonic spasms of the right facial nerve distribution, with contracture of the orbicularis oculi and levator anguli oris. This phenomenon is in contrast to sluggish contracture of the upper eyelid observed by Danzer [12] in complete facial paralysis. It should be recalled that tetanic spasms may be intermittent or, as in this case, continous and without relaxation. In addition, it is recognized that insufficiently treated local tetanus may become generalized. Andrewes [13] believed that in all local cases exhibiting trismus the patient should receive intraspinal treatment, whereas most writers are now in accord that all patients should receive at least one intrathecal injection. The most significant experimental investigation of local tetanus, that of Ransom,[14] pointed to the predominance of the direct action of tetanus toxin on muscle fibers in producing and maintaining contraction. Evidence was presented, however, which indicated that the action of toxin on the central nervous system played a minor but indispensable rôle in establishing the circuit of spasticity.

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10. Slimon, J. G.: Tetanus Complicated by Facial Paralysis, Brit. M. J. **2**:200 (July 30) 1932.

11. Grant, R. L. T.: Kopftetanus, M. J. Australia **2**:512 (Oct. 22) 1932.

12. Danzer, M.: Characteristic Sign in Facial Nerve Paralysis, J. A. M. A. **99**:1416 (Oct. 22) 1932.

13. Andrewes, F. W.: On the Intrathecal Route for the Administration of Tetanus Antitoxin, Lancet **1**:682 (May 5) 1917.

14. Ransom, S. W.: Local Tetanus: A Study of Muscle Tonus and Contracture, Arch. Neurol. & Psychiat. **20**:663 (Oct.) 1928.

SUMMARY AND CONCLUSIONS

1. A case of local (cephalic) tetanus with recovery is recorded.

2. The comparative frequency of this condition is indicated by the large number of cases reported since the World War.

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AN UNDIFFERENTIATED MÜLLERIAN DUCT IN A MAN

AN UNUSUAL CONGENITAL ANOMALY AS A COMPLICATION OF AN INGUINAL HERNIA

JAMES HARRY HEYL, M.D.
NEW YORK

This case of a persistent müllerian duct is reported for its embryologic interest and rarity. That this anomaly occurs is now well known. However, this case merits recording, as only one identical case has appeared since, and to the best of my knowledge, none previously. While I cannot be dogmatic in my interpretation, I feel justified in the belief that this case showed the persistence of an undifferentiated müllerian duct in an adult male.

Several years ago this strange abnormality was encountered by the late Dr. Charles H. Peck in the course of a routine operation for a recurrent inguinal hernia at the Roosevelt Hospital. My interest was revived by the report of a similar case three years later by Dr. Rudolph Matas, in the *Surgical Clinics of North America.*

Dr. Peck granted me permission to secure new pathologic sections from the original tissue. I discussed the sections with the late Dr. G. S. Huntington. He agreed with me that, judging by the position and histology, the anomaly might be a persistent müllerian duct. He did not feel, however, that the possibility of an accessory vas deferens could be ruled out, as he had encountered one some time previously. A drawing of the dissected specimen is appended. No other report of such a case could be found.

Several reported diagnoses of persistent müllerian ducts were proved to be erroneous. With one exception the structures were accessory ureters of an unusual type. Their retention under that title has resulted in much confusion in current literature as to the etiology of accessory ureters. This confusion is inexcusable in view of the excellent work done in this field, notably that of the late Dr. Huntington.

In the absence of other cases of persistent müllerian ducts of similar type, it is necessary to establish the possibility here formulated, briefly to review the subject of the persistence of the müllerian duct in the male in the lesser and more complete stages of differentiation.

REPORT OF A CASE

An unmarried man, aged 32, entered the Roosevelt Hospital in April 1919, in the service of the late Dr. Charles H. Peck, for the repair of a right recurrent inguinal hernia.

The history was not noteworthy except for an attack of gonorrhea in 1908 and a previous operation at another hospital on Aug. 8, 1911, for right inguinal hernia and "acute hydrocele." He was discharged from that hospital as cured on September 12, with the history of a wound infection and swelling of the testicles.

The hospital records of this operation were scanty and inaccurate. The operative findings were described as "a double acute hydrocele with edematous

Fig. 1.—Except for the added length of the anomaly, this illustration from Dr. Matas' case would suffice for Dr. Peck's. "The 'diverticulum' is represented as it presented itself on opening the hernial sac, as a part of the spermatic cord in a congenital hernia." (Reproduced from Surgical Clinics of North America [**2**:1155, 1922].)

thickened tissues and a left hernia." Elsewhere the hernia was correctly described as right. The history mentioned a recent painful swelling of the testicles, and this condition was mentioned also in the report of the physical examination. The operative treatment of the hydrocele was not mentioned; the history suggested

an epididymitis. Whether true hydrocele was present or whether the malformation was present with the "edematous thickened tissues" must remain conjectural.

Examination on entrance to the Roosevelt Hospital showed the scar from the former operation over the right inguinal canal, an enlarged external ring and a

Fig. 2.—Low power photomicrograph showing cross-section of wall of duct. Note the large caliber of blood vessels, especially in the submucosa, and the thick muscular wall. The rectangle at the mucosal surface shows the site of the high power photomicrograph.

moderate-sized elastic mass, which descended into the scrotum when the patient coughed or strained. I found no other abnormality except scattered râles at the bases of the lungs, which were attributed to chronic bronchitis. No feminine characteristics were noted.

The patient was operated on on April 17, 1919, by Dr. Peck under nitrous oxide-ether anesthesia. A medium-sized sac was readily found; it was dissected free, transfixed, ligated and divided at the base. With considerable difficulty the vas and cord were dissected free and isolated from a large tubular structure. The vas was found to be severed at one point, the cut ends being separated about ½ inch (1.27 cm.) and buried in scar tissue. Further dissection revealed a normal pampiniform plexus and a large thickened, tubular structure, parallel to the other structures of the cord, ascending from the middle of the inguinal canal through the internal ring and palpated to the base of the bladder. This anomaly was carefully dissected from the other structures. It ended blindly at the distal end. Its diameter was about one-half inch and was uniform as far as it could be traced. It was thick-walled and hollow, and filled with a mucinous secretion, like the white of an egg. This structure could not be identified at

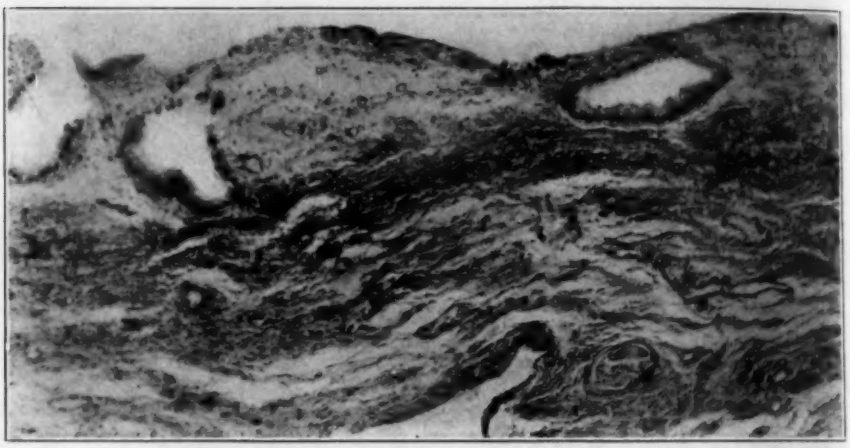

Fig. 3.—High power photomicrograph of the wall of the duct, showing the mucosa and submucosa. The epithelium and type of glands are seen in greater detail.

the time, but as it appeared to have contributed to the hernia and its recurrence, it was ligated and divided as high as possible, and the proximal stump was dropped back in the pelvis. The vas was left beneath the internal oblique muscle. The remaining structures of the cord were transplanted. The closure was made in the usual modified Bassini manner, with transplantation of the pampiniform plexus.

Except for considerable swelling of the right testis the patient's convalescence was uneventful, and he was discharged as cured in May 1919. Every effort to trace him after his discharge was futile.

The microscopic examination of this remarkable structure was extremely interesting. It proved to have an internal lining of mucous membrane. This consisted of high columnar epithelium, with an occasional simple, tubular, glandular arrangement. The glands extended a short distance into the basement mem-

brane, consisting of connective tissue in a network arrangement containing a few lymphoid cells and an occasional polymorphonuclear leukocyte. Beneath the mucosa was an arrangement of tissue in bundles running in various directions. This thick layer had undergone a marked hyaline degeneration, and from its arrangement was probably muscular. The mucosa was well supplied with blood vessels, and there were large vessels in the deeper layers.

MATAS' CASE

Matas' case is remarkably similar:

A man was operated on for hernia. He had had no previous operative intervention. The report of the operation is as follows[1]:

"The most interesting feature of the operation at this stage was the appearance of a long tubular mass which bulged prominently into the hernial sac and extended the full length of the spermatic cord. It began about one inch above the epididymis, extending upward as a component of the spermatic cord into the inguinal canal, and beyond the internal ring, thence backward and downward, following the course of the vas deferens to the base of the bladder, where it was apparently lost in the right seminal vesicle and prostate. It was entirely extraperitoneal, but most intimately adherent to the posterior layer of the sac, which was extremely thin, making it difficult to detach it from the underlying components of the cord.

"This anomalous mass was first seen projecting through the thin translucent posterior layer of the sac, and had the appearance of a long narrow sausage. At first it was taken to be a chronically inflamed spermatic plexus, enlarged and indurated by thrombophlebitis. On further investigation and dissection the enlargement of the cord was found to be due to the presence of this anomalous structure or organ which could not be identified with any of the normal components of the cord. It was blended and fused most intimately with the vas deferens, and the vessels of the cord were displaced and bound together behind it. An incision was made longitudinally into it and parallel with its long axis. This at once opened a hollow tube which, beginning about one inch from the testicle, ran along the cord to the level of the internal ring where it disappeared in the retroperitoneal connective tissue. A no. 10 (English) soft rubber catheter was introduced into the lumen of the tube and it traveled easily and without resistance beyond the internal ring, a distance of seven or eight inches where it met with a resistance and would go no farther. No fluid or secretion of any sort escaped from the catheter when it was withdrawn, showing that the abnormal canal was not a diverticulum of the bladder as had been suggested. Only a long string of clear glairy mucus followed the extraction of the catheter.

"The extra-abdominal part of the diverticulum from its blind terminus in the scrotum up to the level of the internal ring was fully 3½ inches in length, about half the thickness of the little finger and formed a distinct, well-lined, glistening mucus canal of a bluish white color. The mucous canal easily admitted a

1. Matas, R.: A Rare Anomaly Found in a Congenital Right Inguinal Hernia; a Tubular Diverticulum or Prolongation of the Right Seminal Vesicle, Extending into the Scrotum as a Component of the Spermatic Cord, S. Clin. North America **2**:1155, 1922.

no. 12 E. catheter, and was wrapped up in a thick, easily differentiated muscular coat covered by an areolar layer, which together gave the wall of the tube an even thickness of at least ¼ inch. With the finger introduced into the peritoneal cavity through the hernial canal the outline of this tubular cord could be easily traced over the peritoneum and followed to the base of the bladder. The same

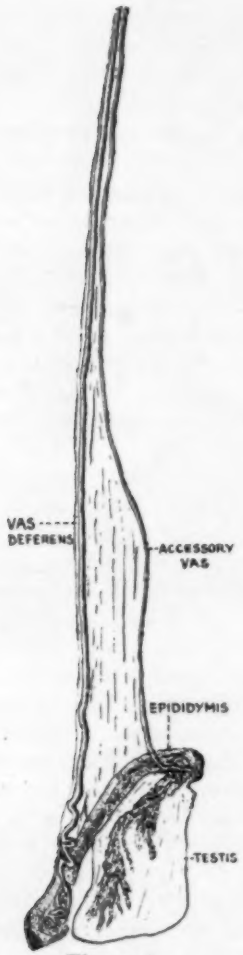

Figure 4

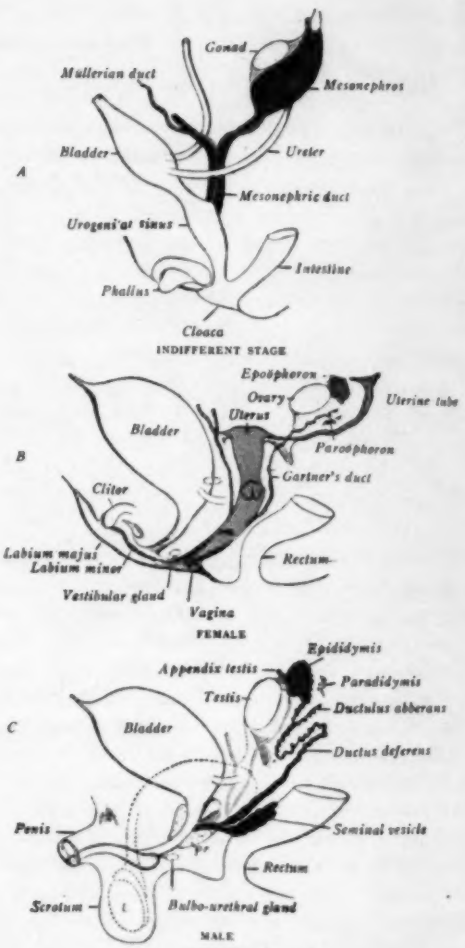

Figure 5

Fig. 4.—Accessory vas deferens into which injections of mercury have been made (illustration supplied by the Anatomical Museum of the Columbia University College of Physicians and Surgeons).

Fig. 5.—Müllerian and wolffian ducts.

impression was conveyed when the diverticulum with the attached vas deferens was followed as far as the finger could reach into the pelvis through the perivesical extraperitoneal space."

COMMENT

Matas was unable to find a similar case in the literature. He concluded that the most likely explanation for the anomaly was that a seminal vesicle had been carried down through the inguinal canal with the descent of the testis. I requested a section for histologic study, but unfortunately, owing to a removal of the hospital, no slides or histologic report could be obtained.

Hypothetically, there appear five reasonable possibilities: (1) an anomaly due to a previous operation or hydrocele, (2) a diverticulum of the bladder, (3) a seminal vesicle, (4) an accessory vas deferens and (5) a persistent müllerian duct.

1. The large size of the anomaly and the identification of a normal vas in the operation rule out its artificial production by operative intervention or occlusion of the vas. The patient in Matas' case had not previously been operated on. It is impossible to conceive of a hydrocele of the cord giving a gross or microscopic picture such as that illustrated.

2. Diverticulum of the bladder may be excluded on the basis of the histology as well as the inability at the time of the operation to demonstrate a connection with the cavity of the bladder.

3. The seminal vesicle might descend with the testis, as was suggested by Matas in the discussion of his case. The histology, however, is somewhat different from that of a seminal vesicle, nor have I found a satisfactory basis for such an abnormality on embryologic or phylogenetic grounds. The seminal vesicles arise in the embryo as lateral diverticula budding from the caudal end of the wolffian ducts in the same location in which they are found in the later and final stages of development. At no time do they come into intimate contact with the testis. It is difficult to see how the descent of the testis could influence the position of the abnormality; nor is there any other developmental reason for its appearance in the inguinal canal.[2]

4. As is shown in the accompanying illustration (fig. 4), an accessory vas deferens might be present, branching off near the prostate and paralleling the vas. As far as can be determined, no such condition has been described in the literature, although this anomaly was known to the late Dr. Huntington, who dissected the specimen illustrated. He also possessed a corrosion specimen obtained from one of the lower animals of the lizard group, illustrating the phylogenetic

2. (*a*) Huntington, G. S.: The Genetic Interpretation and Surgical Significance of Some Variations of the Genito-Urinary Tract, Harvey Lecture, Philadelphia, J. B. Lippincott Company, 1906-1907, p. 235. (*b*) Keibel, F., and Mall, F. P.: Manual of Human Embryology, Philadelphia, J. B. Lippincott Company, 1910-1912.

grounds for this anomaly. He had encountered several cases in the dissecting room. The extreme rarity of the anomaly is probably due more to the failure to search for it than to its infrequent occurrence. It is a condition to bear in mind in operations for sterilization, or in injury or disease of the vas deferens. On examining the slide, Dr. Huntington did not feel that there was sufficient evidence for excluding this possibility or that of a persistent müllerian duct. It is perhaps worth noting that the accessory vas illustrated is smaller than the normal vas, whereas the anomaly is much larger.

5. One hypothesis is left, which I believe to be the most probable explanation for this unusual structure, namely, a persistent müllerian duct, although I concede the remote possibility discussed in the preceding paragraph. One is immediately struck by the similarity of the epithelium of the structure to that lining the uterus and tubes. The glandular arrangement is similar to that of the fundus uteri. The large blood vessels and thick muscular coat also support the analogy. The hyaline degeneration strengthens the belief that this is a rudimentary or nonfunctioning organ. Its anatomic position is also in accordance with this hypothesis.

Its location and relationship correspond with the present knowledge of the development of the müllerian duct. It is generally acknowledged by embryologists that the nonpedunculated hydatid which is found near the upper pole of the testis represents the remnant of the cephalic end of the müllerian duct, while the utriculus prostaticus located near the middle of the posterior surface of the prostate represents the caudal end of the müllerian duct in the male. Assuming its persistence, it would follow that the descent of the testis would carry the duct into the position occupied by the anomaly. An analogous condition in the female is that of an indirect inguinal hernia in which the ovary has descended through the enlarged canal of Nuck into the labia majora, carrying the cephalic end of the tube with it. The tube in such a case represents the differentiated müllerian duct.

Eight cases were found in the literature under the title of persistent müllerian ducts. Investigation reduced these to six: (1) Boogard's,[3] 1876, which was described by Pouchet;[4] (2) Barth's,[5]

3. Boogard, J. A.: Persistencie der Müllersche gangen bij een wassen man, Verhandl. d. k. Akad. v. Wetenach, Amsterdam **9**:266, 1876.

4. Pouchet, G.: Persistence du canal de Müller chez l'homme adulte, J. d'anat. et de physiol **13**:200, 1877.

5. Barth, M.: Anomalie de développement de l'utricule prostatique; persistance de l'organ de Müller du côté droit, en forme de poche diverticulaire passant sous la vessie; soulèvement de la muqueuse vésicale formant valvule (retention d'urine; dilation consécutive des uretères et hydronéphrose double), Bull. Soc. anat. **53**:483, 1878.

1879, the subject of papers by Rémy [6] and Moutard-Martin [7]; (3) Ord's,[8] 1879; (4) Reliquet's,[9] 1887; (5) Nicolich's,[10] 1905, and (6) Martin's,[11] 1878. The first five can be discussed under the same head, as they are similar except for unessential details. All were found at autopsy and all were in males from childhood to middle age. Some were bilateral, and others unilateral. In every case the ducts arise from a body situated above the upper pole of the kidney; they parallel the ureter and are attached below the ureteral orifice and bladder in the region of the verumontanum of the urethra, a definite communication being noted in some of the cases with the urethra at this point. This anomaly resulted in an obstruction near the neck of the bladder which caused hydronephrosis and uremia and which was the direct cause of death. No microscopic studies were reported of any of these cases. Boogard noted that the upper end of the canals had remained in relation with the kidneys and had not followed the testicles in their migration.[5] Pouchet [4] and Rémy [6] argued from that that the nonpedunculated hydatid was not a remnant of the müllerian duct. Rémy [6] had found the hydatid in its usual position on the testis on the same side as the duct in the case of Barth. The verdict of time, however, has preserved the origin of the nonpedunculated hydatid. Pouchet's argument that these ducts could not be ureters because they were not connected with the kidneys and emptied into the urethra has likewise been proved erroneous. Ord noted that the body above the kidney "had the structure of a renal organ with evidence of contraction and degeneration." [8] Reliquet at first considered his case to be one of an accessory ureter, but was led to reverse this belief by Duval, who was familiar with the case of Barth.[5] One is immediately struck by the similarity to a rare but well known type of accessory ureter with an accessory kidney to which they conform in every respect. The embryologic basis for this type of ureter was explained by the late Dr. Huntington in the Harvey Lecture of 1906, delivered at the

6. Rémy, C.: Sur l'utricle prostatique et les canaux de Müller chez l'homme, J. d'anat. et de physiol. **15**:175, 1879.

7. Moutard-Martin, R.: Cas de persistance du conduit de Müller avec anomalie de développement de l'utricle prostatique chez un enfant de six ans, Bull. Soc. anat. de Paris **54**:529, 1879.

8. Ord, W. M.: Malformation of the Genital Organs of a Man with Persistence of One of the Ducts of Müller, M. Times & Gaz., London **2**:654, 1879.

9. Reliquet: Persistance du canal de Müller. Hydronéphrose du rein et de l'uretère droit. Pyelonéphrite calculeuse du rein gauche très hypertrophie, Progrès med. **5**:205 and 230, 1887.

10. Nicolich, G.: Persistance de conduit de Müller, Assoc. franç. d'urol, Proc. verb. **8**:580, 1905.

11. Martin, E.: Mémoire sur un cas de persistance des canaux de Müller, J. d'anat. et de physiol. **14**:21, 1878.

New York Academy of Medicine. He described it as a complete reduplication of the ureter and vesical termination of one duct, while the other duct empties, in association with the ejaculatory duct, into the prostatic urethra.[2a] The case of Nicolich, the last to be reported, was presented before the Association française d'urologie in 1905. Dr. J. Albarran, who was present, objected to the diagnosis of Nicolich, pointing out in the gross specimen the similarity of the duct to the ureter; the cortex of the accessory kidney, which Nicolich had believed to be a congenital gland, presumably an ovary. It is also significant that no similar cases have been reported as showing persistence of the müllerian duct since that time. On these grounds I feel justified in denying the authenticity of these cases as instances of müllerian ducts.

The case reported by Martin was that of a 7 or 8 month fetus, with an enormously distended bladder, no trace of urachus or urethra, an imperforate anus, no vaginal canal or genital glands and two tubes running from the region of the kidneys to the bladder, parallel and internal to the ureters.[11] The undeveloped external genitalia were suggestive of the female. If one accepts the assumption that these tubes are müllerian ducts, one would also be justified in assuming that this was a female fetus, as otherwise it was entirely sexless. In any case, the monstrosity does not come within the confines of this paper.

In the absence of identical cases, it becomes necessary briefly to review the question of hermaphrodism.

It will be recalled that at an early stage of fetal life every person is potentially bisexual. The primitive genital glands of both sexes arise in the genital ridge. Two tubular structures appear on both sides—the wolffian duct and the müllerian duct. In the male the gland at an early stage develops into the testis. The vas deferens, the seminal vesicles and the epididymis are formed from the wolffian duct. Normally the müllerian duct atrophies and leaves only vestigial remains, namely, the canals of Rathke, the nonpedunculated hydatid and the prostatic utricle. The nonpedunculated hydatid, when present, is found on the testicle and represents the remains of the cephalic end of the müllerian duct; the prostatic utricle near the center of the posterior surface of the prostate represents the caudal end.[2b]

In the female the müllerian ducts of the two sides fuse at the lower end and eventually form the upper part of the vagina, cervix, corpus uteri and fallopian tubes. The remnants of the wolffian ducts are represented by the canals of Gartner, the longitudinal canal of the organ of Rosenmüller and the hydatid of Morgagni.[2b]

Hermaphrodism is a subject of myths and early art of almost all races from the earliest times. The early reported cases were bitterly contested, and every possible and some impossible objections were voiced against any one so rash as to report a case. In 1896 Blacker

and Lawrence [12] reported a case and reviewed twenty-eight cases, of which they considered Heppner's bilateral case, and Obolensky's and Schmorl's unilateral cases and their own case as proved. Blacker and Lawrence's slides were reviewed by two eminent pathologists, who agreed that the patient was not a hermaphrodite, but, parodoxically, one claimed that it was undeniably a female, while the other considered that it was a male. To Simon must go the credit for placing the diagnosis on an indisputable footing and ending the controversy for all time. He reported a case of Gané and reviewed the cases of Salen and of Blacker and Lawrence, which he accepted without reservation; the three cases mentioned earlier were acceptable to him with some reservations.[13] Since Simon's report many more cases have been added.

True hermaphrodism in the sense of functional glands of both sexes with accessory organs has never been reported in any vertebrate, although it is not uncommon in the lower forms of animal life. There is some unknown controlling factor which prevents the coincidental development of functioning glands of both sexes in a single person. One might apply the old definition of a poison to hermaphrodism: Every one or no one is a hermaphrodite, it being a question of degree.

The so-called true hermaphrodism of Klebs [14] is based on the findings of glands of both sexes, identifiable microscopically and morphologically, in one person. These glands may be bilateral or unilateral, or the two may be incorporated together in an ovotestis. The ovotestis is interesting surgically from the occasional tumors arising in the nonfunctioning gland.

In addition to the glandular hermaphrodites, many cases are reported of tubular hermaphrodites. For example, a person may have the glands of one sex and at the same time bear the tubular accessory structures of both sexes. These persons are usually termed tubular pseudohermaphrodites. Obviously, the glandular and tubular hermaphrodites may be combined, which gives the nearest approach to an actual hermaphrodite. Even in these combined cases the sex may be determined, if one can ascertain which of the glands are functioning.

The pseudohermaphrodites again vary from the completely differentiated structures of the opposite sex to an approach to the vestigial remains which are normally found in most persons.

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12. Blacker, G. F., and Lawrence, T. W. P.: A Case of True Unilateral Hermaphroditism with Ovotestis Occurring in Man, with Summary and Criticism of the Recorded Cases of True Hermaphroditism, Tr. Obst. Soc. London, 1896, **38**: 265, 1897.

13. Simon, W.: Hermaphroditismus versus, Virchows Arch. f. path. Anat. **172**:1, 1903.

14. Klebs, E.: Handbuch der pathologischen Anatomie, Berlin, A. Hirschwald, 1873.

I shall limit the consideration to the male pseudohermaphrodite with the persistent müllerian duct. The cases reported by Simon and many others since that time have shown that an ovary and the completely differentiated müllerian duct may exist in an otherwise normal male. Many cases have been reported of males with persistence of the müllerian duct in the completely differentiated state without ovarian tissue. This has been described as a predisposing cause of hernia. Many of these cases were discovered through the finding of these derivatives in a hernial sac.

Duse [15] collected fifteen cases of masculine pseudohermaphrodites with persistent differentiated müllerian ducts associated with hernias, and LaHaye added seven more in 1920, with an interesting résumé on the subject of hermaphrodism.[16]

There is a wide gap between this condition and the condition which has been described as an enlargement of the prostatic utricle. These vary from a scarcely perceptible enlargement of the utricle to a condition in which one or two small, short tubes or solid strands of tissue arise from the enlarged utricle. A case reported by Young and Cash is representative of this group.[17]

I believe that Dr. Peck's and Dr. Matas' cases are an intermediate and connecting link between the two types of male pseudohermaphrodites described earlier. In the lower animals a similar condition has been reported in moles, beavers and frogs.[16] I prefer the term "persistence of the undifferentiated müllerian duct in a male" to distinguish such cases as ours from the other types of persistence, as they form a distinct clinical entity.

It would be expected that cases such as ours would occur numerically in an intermediate position between the instances of differentiated müllerian duct and the cases of enlargement of the prostatic utricle, as these approach the normal state. I can account for the disparity of reported cases only on the basis that practically all of the male pseudohermaphrodites with the differentiated female accessory structures are reported, owing to the easy recognition of the condition and its dramatic possibilities, and that cases like ours are not reported. If my diagnosis is correct, I should expect that more cases will be reported in the future. There is nothing in the histologic picture which would not fit this hypothesis.

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15. Duse, A.: Utero masculino erniáto con distopia traversa del testicolo sinistro, Clin. chir. **18**:1597, 1910.

16. LaHaye, P.: Reflexions au sujet d'un cas d'hermaphroditisme tubulaire masculine interne, Thèses de Paris, 1919-1920, p. 29.

17. Young, H. H., and Cash, J. R.: A Case of Pseudo Hermaphroditismus Masculinus, Showing Hypospadias, Greatly Enlarged Utricle, Abdominal Testis, and Absence of Seminal Vesicles, J. Urol. **5**:405 (May) 1921.

As both of the cases described were discovered in the course of repair of hernias, hernia seems to be a predisposing factor in the causation of the anomaly. It is also interesting to note that the treatment adopted by two master surgeons was the same, although neither had seen a similar condition. The recurrence in our case was probably due to the failure to excise the anomalous structure at the first operation.

CONCLUSIONS

1. The cases described I believe to be instances of undifferentiated persistent müllerian ducts in adult males, though I admit the remote possibility that the anomalies are accessory vasa deferentia.

2. The cases reported to show persistent müllerian ducts, with one exception, proved to be cases of accessory ureters and accessory kidneys.

3. This condition is a predisposing cause of hernia.

4. The proper treatment, if these anomalies occur with hernia, is excision to prevent recurrence.

5. A link is added between the enlarged prostatic utricle and the differentiated müllerian duct.

6. A case of an accessory vas deferens is cited with illustration.

NOTE.—The late Dr. Charles H. Peck permitted me to report this case, and Dr. James I. Russell renewed this consent. The late Dr. George S. Huntington assisted in the investigation, and Dr. A. R. Stout reviewed the histology. Mr. Frederick Kraus made the translation from the German.

ANOMALIES OF INTESTINAL ROTATION AS A CAUSE OF INTESTINAL OBSTRUCTION

REPORT OF TWO PERSONAL OBSERVATIONS; REVIEW OF ONE HUNDRED AND THREE REPORTED CASES

CLARENCE E. GARDNER JR., M.D.
AND
DERYL HART, M.D.
DURHAM, N. C.

In the practice of abdominal surgery a clear conception of the various possibilities of derangement of intestinal rotation and fixation is essential. Anomalies in position of the intestinal tract may exist without symptom and manifest themselves incidentally at operation. Because of the bewildering disposition of the viscera the operation may be unnecessarily prolonged or the ultimate object abandoned. Under other conditions, because of the abnormal position of the cecum, a patient with acute appendicitis may be watched until perforation has occurred. Of greater importance to the surgeon, however, are the forms of intestinal obstruction secondary to torsion or kink, dependent on abnormalities of intestinal rotation and fixation. Since many of these obstructions are chronic and date from birth, and since the surgeon usually sees the patient only in consultation, it is equally important for the internist and the pediatrician to be familiar with this characteristic clinical picture.

The occurrence in our practice within one month of 2 cases of volvulus of the entire mesentery secondary to anomalies of intestinal rotation and fixation and the appearance of frequent reports of similar cases in the literature of recent years make it evident that the condition is more frequent than is generally accepted. It is the purpose in this report (1) to review the stages in normal intestinal rotation and the possibilities of abnormality in each, (2) to present our 2 cases and (3) to review the literature on anomalies of intestinal rotation as a cause for the development of acute and chronic intestinal obstruction.

EMBRYOLOGIC DEVELOPMENT

Although much of the embryologic development of the intestinal tract was known and described as early as 1817 by Meckel [1] most of our present knowledge of intestinal rotation dates from the work of

From the Department of Surgery, Duke University School of Medicine.

1. Meckel, J. F.: Blindungsgeschichte des Darmkanals der Säugetiere und namentlich der Menschen, Deutsche Arch. f. Physiol. **3**:1, 1817.

Mall [2] in 1898 and of Frazer and Robbins [3] in 1915. We have drawn freely from the latter two sources and from Dott's [4] masterful article published in 1923.

At the end of the fifth week of intra-uterine life the abdominal portion of the intestinal tract may be schematically represented as in figure 1. The entire alimentary tract is suspended in the midline by a common dorsal mesentery. The tract is divided into three parts according to form and blood supply: the foregut forming the upper loop supplied by the celiac axis, the midgut forming the umbilical loop supplied by the superior mesenteric artery and the hindgut or lower loop supplied by the inferior mesenteric artery. The midgut grows rapidly, and by the end of the fourth week the vitello-intestinal duct has lost its connection with the yolk sac and umbilical cord. Available intra-abdominal space is so diminished by the rapid growth of the liver and the midgut loop that the latter is extruded into the root of the umbilical cord as a temporary and physiologic umbilical hernia. At the fifth week the midgut loop still lies in the sagittal plane, the apex of the loop being represented by the remnant of the vitelline duct and the termination of the superior mesenteric artery. The anterior segment of this loop is termed the prearterial segment, and the posterior, the postarterial segment.

At an early period the lower end of the foregut and the upper end of the hindgut become fixed points from which the midgut loop is suspended. The upper part of the duodenum is deviated to the right by the bulging and unequal growth of the greater curvature of the stomach. It becomes fixed in this location by the thickening and shortening of its mesentery and by the outgrowth of the pancreatic rudiment. From the upper end of the hindgut a retention band passes upward as a thickening in the mesentery to the region of origin of the superior mesenteric artery. This band does not keep pace in growth with the gut or remainder of the mesentry and thus fixes the intestine at the junction of the midgut and hindgut. These two fixed points are close together, and the growth of the embryo causes their further approximation. The narrow isthmus which they form and from which the midgut loop hangs is called the duodenocolic isthmus. This early fixation of foregut and hindgut loops precludes the possibility of either loop taking part in intestinal rotation which is entirely confined to the midgut. Errors in disposition of the foregut or of the hindgut are rare.

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2. Mall, F. P.: Development of the Human Intestine and Its Position in the Adult, Bull. Johns Hopkins Hosp. **9**:197, 1898.

3. Frazer, J. E., and Robbins, R. H.: On the Factors Concerned in Causing Rotation of the Intestine in Man, J. Anat. & Physiol. **50**:75, 1915.

4. Dott, N. M.: Anomalies of Intestinal Rotation: Their Embryological and Surgical Aspects, with Report of Five Cases, Brit. J. Surg. **11**:251, 1923.

The process of intestinal rotation is divided by Frazer and Robbins[8] into three stages. The first includes the time during which the midgut loop occupies the umbilical hernia and until it is returned to the abdominal cavity at about the tenth week. The second stage occupies the time during which rotation and reduction of the midgut into the abdominal cavity take place and is completed when the cecum reaches the right loin in the eleventh week. The third stage extends from this

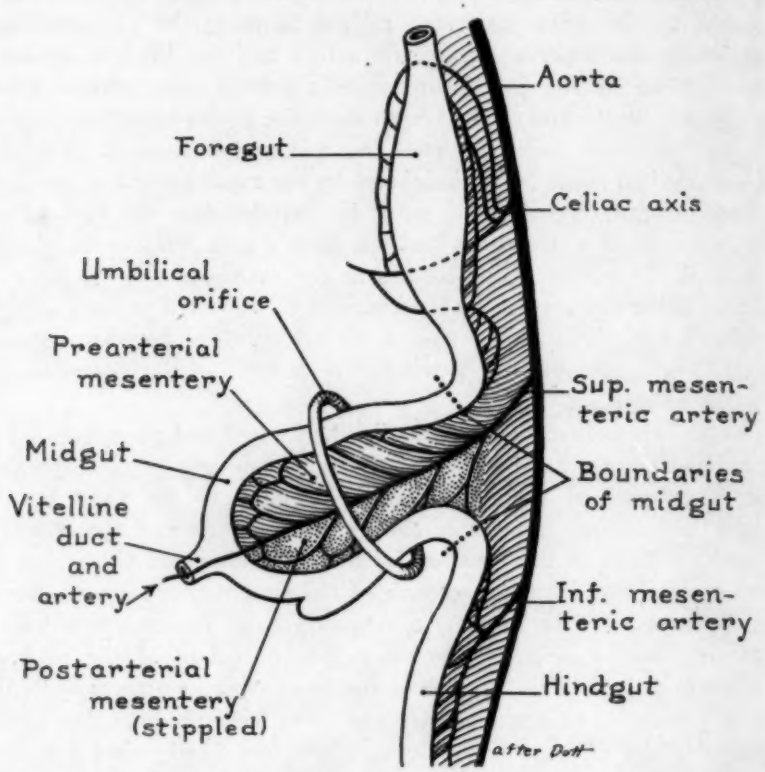

Fig. 1.—Diagram of the alimentary tract at the fifth week of intra-uterine life (lateral view). The foregut, midgut and hindgut are shown with their individual blood supply supported by the common dorsal mesentery in the sagittal plane. The midgut loop has been extruded into the umbilical cord.

time until shortly after birth. It is characterized by descent of the cecum and by fixation of the cecum and lower part of the duodenum by fusion of their mesenteries with the posterior parietal peritoneum. The first stage may be considered as a preparation for, and the third as the completion of, the important second stage during which in an exceedingly short time the reduction and major rotation of the intestinal tract occur.

First Stage of Rotation.—The essential feature of the first stage of rotation is the turning of the intra-umbilical loop from the sagittal to the horizontal plane so that the prearterial segment lies to the right and the postarterial segment to the left (fig. 2). This is brought about by the enlargement and down-growth of the liver carrying with it the left umbilical vein which depresses the proximal part of the prearterial segment.

Failure of the intestine to rotate beyond the first stage is seen in exomphalos, in which condition the embryonic hernia into the root of the umbilical cord persists in part or in full until birth. In this condition

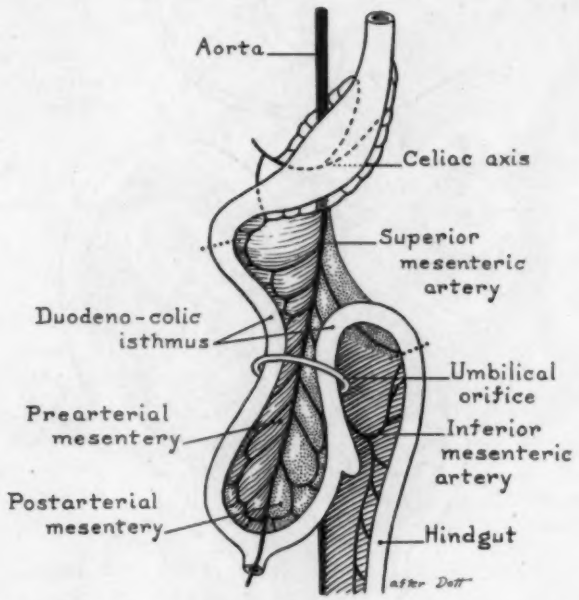

Fig. 2.—Diagram of the alimentary tract at the eighth week of intra-uterine life (anteroposterior view). The first stage of rotation is being completed. Note the narrow duodenocolic isthmus from which the midgut loop depends and the right-sided position of the small intestine and left-sided position of the colon. Maintenance of this position within the abdomen after birth is spoken of as nonrotation.

the hernia is covered by the thin and translucent umbilical cord, in contrast to the covering of skin in the usual umbilical hernia. The sac contains the nonrotated midgut loop occupying a position similar to that found in the embryo at the eighth or ninth week.

Second Stage of Rotation.—This is the stage of reduction and of major rotation of the midgut loop which takes place at the beginning of the tenth week and ends when the cecum reaches the right loin (figs.

3 and 4). This, the most important phase of the process of rotation, occurs quickly, and in none of the specimens studied by Mall or by Frazer and Robbins was the gut found in the process of its return. Frazer and Robbins pointed out that it is not possible for the gut to be returned en masse and that the cecum especially offers resistance to this passage. The proximal limb of the prearterial segment is thought to be reduced first, its coils entering the abdomen in an orderly sequence

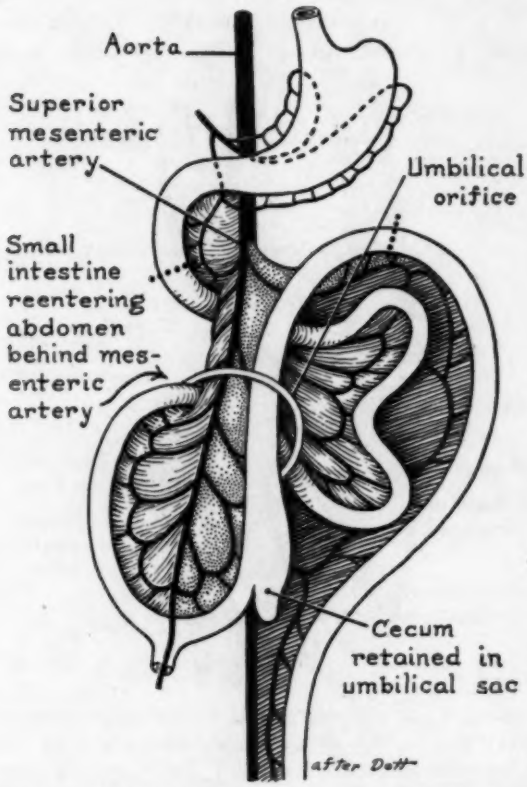

Fig. 3.—Diagram of the alimentary tract at about the tenth week during the second stage of rotation (anteroposterior view). The bowel in the temporary umbilical hernia is in the process of reduction, the most proximal part of the prearterial segment entering the abdomen to the right of the superior mesenteric artery first, and the remainder of the bowel following in orderly sequence. The superior mesenteric artery is held forward close to the abdominal wall by the cecum and ascending colon, permitting the bowel to pass under it. As the coils of small intestine collect within the abdomen the hindgut is displaced to the left and upward.

to the right of the superior mesenteric artery. As these coils collect within the abdominal cavity, the hindgut and its mesentery, which lie in the midline, are displaced to the left, backward and upward. The

splenic flexure and descending colon are thus carried into their normal position (fig. 3). The cecum and adjacent colon are reduced last. As they enter the abdomen and the colon straightens itself out they are deflected to the right (fig. 4). The final result of the second stage is seen to be a contraclockwise rotation of the midgut loop about the

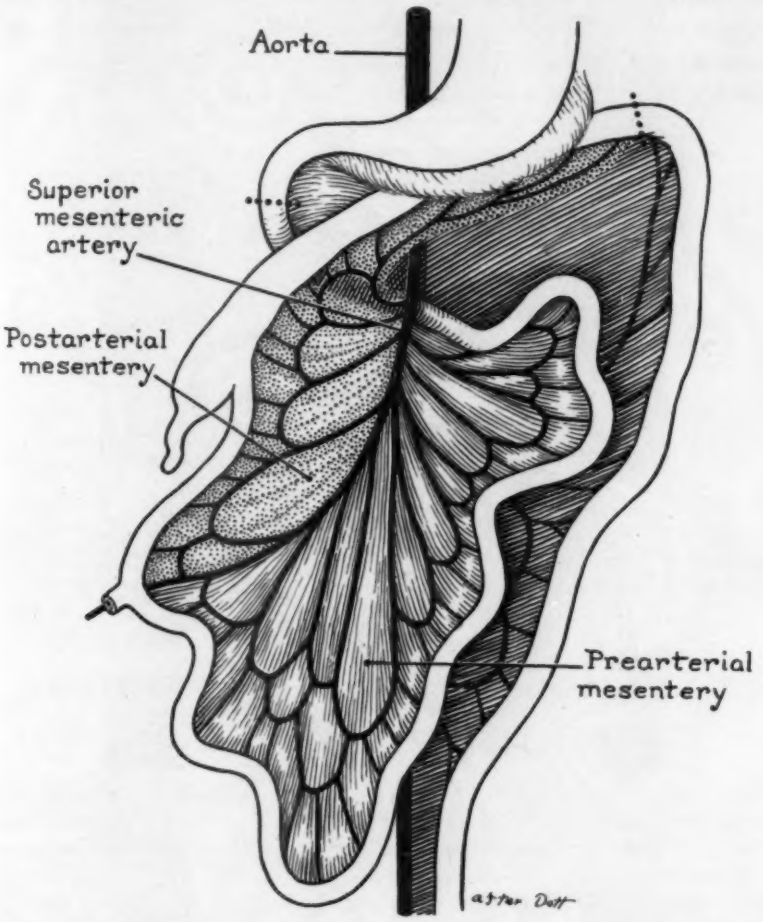

Fig. 4.—Diagram showing the condition of the alimentary tract at the end of the second stage of rotation (eleventh week). From its original sagittal position the midgut has rotated 270 degrees in a contraclockwise direction about the origin of the superior mesenteric artery. The essentials of the permanent disposition of the viscera have been attained.

axis of the superior mesenteric artery of 270 degrees from the sagittal position of the primitive umbilical loop. In this way the intestinal tract comes to occupy its position as normally seen in the adult, the duodenum

being placed behind the origin of the superior mesenteric artery while the transverse colon crosses the same point anteriorly.

Dott [4] classifies derangements of the second stage of rotation as nonrotation, malrotation and reversed rotation.

Nonrotation.—In nonrotation of the midgut loop (figs. 5, 6 and 7) the intestinal tract occupies a position within the abdomen fundamentally the same as in the embryo at the eighth week (fig. 2). The small intestine lies to the right of the midline and the colon to the left. The duodenum descends to the right of the superior mesenteric artery and is mobile

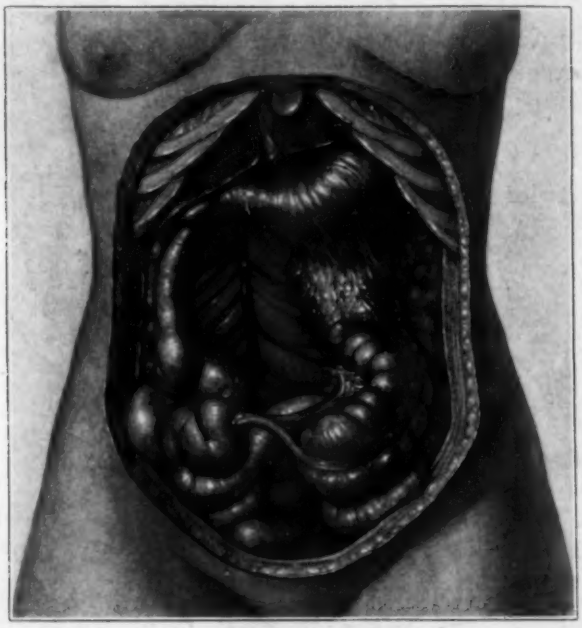

Fig. 5.—Disposition of the intestinal tract as found in nonrotation in the adult. The duodenum remains suspended on its mesentery and occupies a position entirely to the right of the vertebral column. The small bowel occupies the right side of the abdomen and the colon the left, so-called "left-sided colon." The terminal ileum crosses the midline to enter the cecum on its right side. Often a narrow U-shaped loop of transverse colon hangs between the ascending and the descending colon. The entire midgut is suspended on a common mesentery from the narrow duodenocolic isthmus at the origin of the superior mesenteric artery.

on its mesentery. The terminal ileum crosses the midline to reach the "left-sided" colon where it enters the cecum from the right instead of from the left. From this point the ascending colon passes upward on the left of the midline to a point behind the greater curvature of the stomach. Between this point and the splenic flexure is a narrow

Fig. 6.—Nonrotation as seen by roentgen examination of the barium-filled stomach, duodenum and small intestine in a woman aged 63 seen in consultation with Dr. J. M. Ruffin. The anomaly had caused no symptoms. The location of the duodenum and small intestine entirely on the right side of the vertebral column is shown.

Fig. 7.—Same patient as in figure 6. The barium-filled colon is seen entirely on the left side of the abdomen.

U-shaped loop of transverse colon. In this position there may be no secondary fixation of the mesentery, the entire midgut loop hanging free from the narrow duodenocolic isthmus (fig. 2). Such an arrangement predisposes to the development of a volvulus of the entire midgut loop. This occurred in 23 of the cases reviewed.

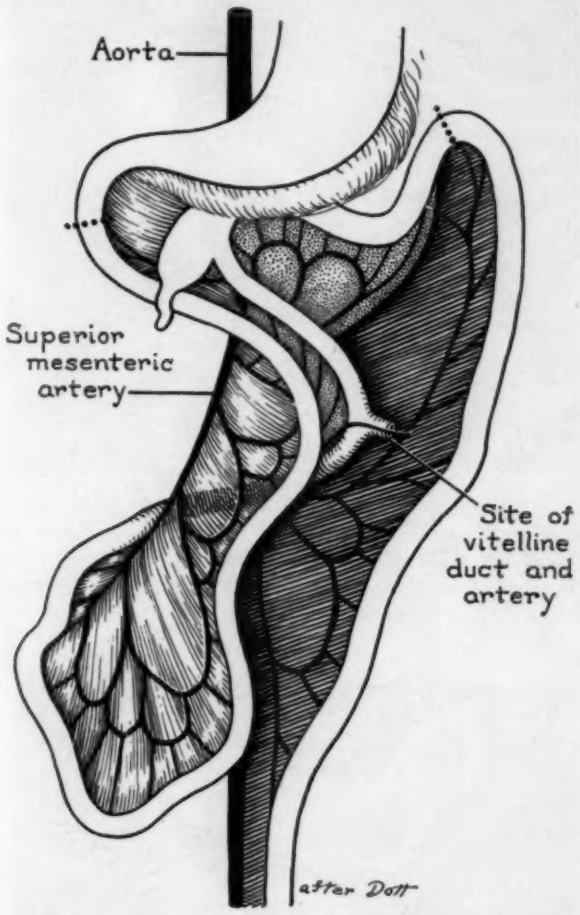

Fig. 8.—Diagram of the alimentary tract in one form of malrotation (anteroposterior view). The prearterial segment has gone through a reversed rotation (clockwise) of 90 degrees, while the rotation of the postarterial segment is arrested.

Malrotation.—By this term Dott designates the irregular defects of rotation and fixation. In one type the prearterial segment is reduced in front of the superior mesenteric artery while the rotation of the postarterial segment is arrested (fig. 8). In another type the prearterial segment has remained entirely on the right side, as in nonrotation, while the postarterial segment has rotated normally but has been prevented

from becoming fixed to the posterior abdominal wall by the presence of the unrotated small intestine. In both of these conditions the cecum and ascending colon retain their primitive mesentery in common with that of the small intestine (mesenterium commune). The attachment of the root of the mesentery to the abdominal wall is very short, and volvulus of the common mesentery may be produced. It is quite possible that with the abnormal mesenteric fixations which accompany these malrotations the intestinal lumen may be constricted. Seven cases have

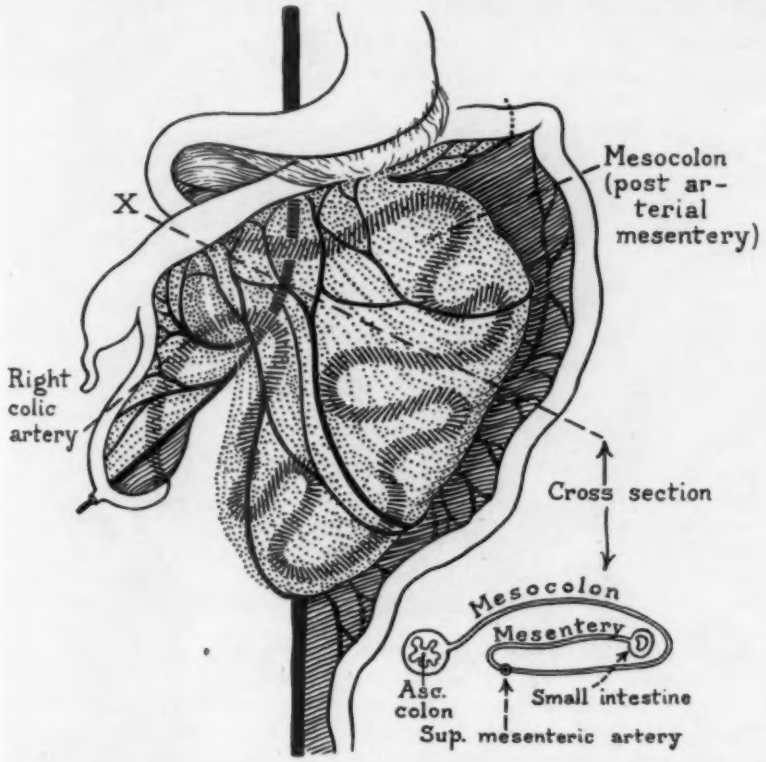

Fig. 9.—Diagram of a form of malrotation in which the small intestine rotates into the mesentery of the postarterial segment between the superior mesenteric artery and the colon (anteroposterior view). The small bowel is thus enclosed entirely in an envelop of peritoneum (after Haymond and Dragstedt).

been observed (table 3) in which there was some obstruction to the duodenum because of such an abnormality.

Another form of malrotation is that in which a massive intra-abdominal hernia is simulated by rotation of the prearterial loop into the mesentery of the postarterial segment between the superior mesenteric artery and the colon. Almost the entire small intestine may be contained in a peritoneal envelop thus formed (fig. 9). Such a con-

dition reported by Haymond and Dragstedt [5] existed without symptoms and was found in a man aged 67, who died of carcinoma of the stomach. Lickley and Cameron [6] reported an almost similar case without symptoms.

Reversed Rotation.—In this condition a 90 degree clockwise rotation takes place instead of the normal 270 degree contraclockwise one. Thus the transverse colon passes dorsally to the duodenum and superior mesenteric artery (fig. 10). If the normal fixation of the root of the mesentery toward the right iliac fossa takes place in this position the transverse colon becomes trapped in a tunnel beneath this acquired attachment. Fixation of the cecum and ascending colon is usually incomplete, and torsion of the mobile right half of the colon with obstruction

Fig. 10.—Drawing showing the conditions found in reversed rotation. The midgut has rotated 90 degrees in a clockwise direction, throwing the transverse colon under the duodenum. As the root of the mesentery becomes fixed the colon is trapped in a tunnel. The ascending colon retains its primitive mesentery, and in this case was obstructed by torsion at the point where it entered the tunnel.

of the transverse colon at the site of the tunnel through the root of the mesentery may readily occur. Ten cases of this kind have been collected (table 2).

Third Stage of Rotation.—This stage is characterized by the descent and fixation of the cecum in its normal position, the fixation of the descending colon and the fixation of the lower portion of the duodenum.

5. Haymond, H. E., and Dragstedt, L. R.: Anomalies of Intestinal Rotation, Surg., Gynec. & Obst. **53**:316, 1931.

6. Lickley, J. D., and Cameron, J.: Note on a Case of Abnormal Disposition of the Peritoneum, J. Anat. & Physiol. **41**:88, 1906.

It is completed about the time of birth. The important feature of this stage is the fixation of the cecum in the right iliac fossa so that the mass of small intestine originally dependent from a narrow pedicle at the origin of the superior mesenteric artery acquires a broad oblique attachment to the posterior abdominal wall. It is the absence of this broad attachment which predisposes to volvulus of the entire mesentery.

Failure of the cecum to elongate and undergo early fixation explains the subhepatic and lumbar positions of this organ. Deficient fixation of the ileocecal segment predisposes to the formation of a volvulus of the cecum or ileocecal segment. No attempt has been made to include any of the latter conditions in this presentation.

REPORT OF CASES

Two cases of volvulus of the entire mesentery secondary to anomalies in intestinal rotation with symptoms of duodenal obstruction are as follows:

CASE 1.—R. B., a white boy, aged 6 years, was admitted to the Duke Hospital in the pediatric service of Dr. W. C. Davison on July 15, 1932, complaining of intermittent attacks of cramping abdominal pain and vomiting since birth. The patient was the eighth of ten children of healthy parents; he had been born spontaneously at term, weighing 8½ pounds (3,854 Gm.) at birth. The first feedings were taken normally. On the third day after birth forceful vomiting of bile-stained material began to occur regularly following each feeding. At the age of 5 weeks the child weighed only 4½ pounds (2,030 Gm.). The mother stated that at that time the fontanels and abdomen were sunken in and the child so feeble that she expected it to die at any moment. For a time thereafter there was improvement. However, from three days after birth until the time of admission the patient had had recurring attacks of abdominal cramps and vomiting of from one to three weeks' duration with intervals between attacks never exceeding five weeks. Development had been normal although he had always been underweight. Attacks were often initiated by overeating, and the accompanying abdominal cramps were usually relieved by vomiting. Bowel movements were scanty but not abnormal during attacks.

The patient was an undernourished boy of 6 years in no discomfort. He weighed 33 pounds (15 Kg.) and was 102 cm. in height. The abdomen was flat and of normal contour. No peristalsis was seen, no tenderness elicited and no masses felt. The superficial veins over the abdominal wall were moderately dilated. Except for evidences of chronic infection in the tonsils the remainder of the physical examination gave normal results.

The hemoglobin was 83 per cent (Sahli); the red blood cells numbered 4,320,000, and the white blood cells, 5,000; the differential count was normal. The tuberculin reaction was positive. The Wassermann test of the blood was negative. The blood calcium was 10.2 mg. per hundred cubic centimeters of blood; the phosphorus, 3.6 mg., and the nonprotein nitrogen, 46 mg. The carbon dioxide-combining power was 67.3 volumes per cent, and the sodium chloride 493 mg. per hundred cubic centimeters on one occasion and 428 mg. on another. Gastric analysis showed: no free hydrochloric acid and 15 combined in the fasting residue; 45 free and 57.9 total acidity after histamine and alcohol.

On July 19 after a barium sulphate meal the first and second portions of the duodenum were found to be enormously dilated (fig. 11) and entirely on the right

of the vertebral column. There was a 25 per cent gastric residue after six hours. This was attributed to an obstruction in the third part of the duodenum. At twenty-four hours the colon was filled and in normal position.

The child remained in the hospital for five and one-half weeks. During this time he suffered seven attacks of cramps in the upper part of the abdomen followed and relieved by vomiting of bile-stained material containing food residue. As operation was not agreed on he returned home on August 26.

Twenty-six days after discharge he was readmitted to the hospital for operation. During the interval he had had almost daily attacks of cramping abdominal pain. There were no changes in the physical findings except for the presence of fulness in the upper part of the abdomen. No peristalsis was visible.

Operation was performed on September 27 by one of us (D. H.). The abdomen was opened through a right rectus incision. The upper part of the abdomen was explored on the right side, and the duodenum was found to be

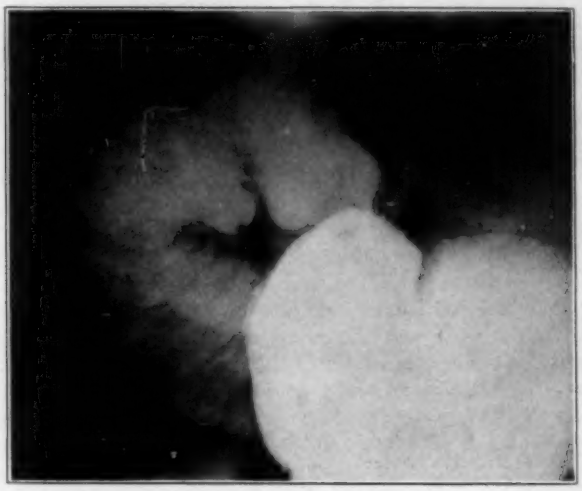

Fig. 11.—Roentgenogram of the barium-filled stomach and duodenum in case 1. The tremendous dilatation of the duodenum is evident. Fluoroscopic examination showed that the duodenum lay entirely on the right of the vertebral column.

dilated. The transverse colon was then lifted up to expose the duodenojejunal junction, but this was concealed by numerous loops of small intestine. It was noted, however, that all the veins to the ascending colon were markedly dilated. The hand was inserted into the abdomen for palpation, and the fingers immediately passed around a tight bandlike structure at the duodenojejunal junction. The exact nature of this structure could not be determined, but on exposing it for inspection it was seen that the cecum was fixed in normal position and that for a distance of about 4 inches (10.16 cm.) the terminal ileum was collapsed and stretched tightly from the ileocecal valve to a point at which it disappeared around the root of the mesentery (fig. 12). The veins to this part of the ileum were extremely dilated. On inspection of the remainder of the small intestine it was seen that the lymphatics were dilated, the lymph nodes greatly enlarged and the veins markedly distended. The tissues were moderately cyanotic. The small intestine was collapsed.

In order to correct the anomaly it was necessary to deliver all of the small intestine. It was then seen that there was a 360 degree clockwise rotation of the root of the mesentery. All of the small intestine was involved except the duodenum and the lower few inches of the ileum (fig. 12). The lumen of the intestine was compressed at the duodenojejunal junction. The mesentery was untwisted, and it was then found that the proximal jejunum and terminal ileum were adherent over a distance of approximately 3 inches (7.62 cm.) (fig. 13). The jejunum and ileum were separated, and the dissection was carried between the mesenteric vessels

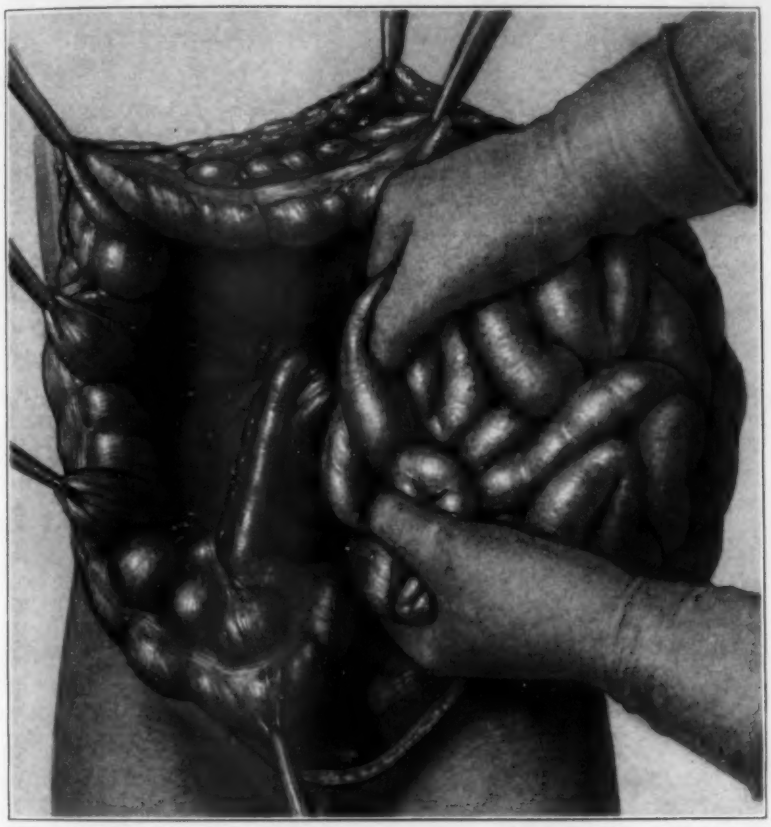

Fig. 12 (case 1).—Appearance on opening the abdomen (from a sketch made during the operation). A 360 degree clockwise rotation of the entire small intestine has taken place. Dilated veins and lymphatic vessels and enlarged lymph glands in the right half of the mesocolon are apparent. The ascending colon has its normal attachment; the duodenum, however, is entirely on the right of the vertebral column.

of the two loops so that the jejunum could be carried into the upper left quadrant and the ileum into the lower right quadrant (fig. 14). The small intestine was then returned to the abdominal cavity so as to lie between the two loops and hold them in the position shown in figure 14. The abdominal incision was closed in layers with catgut for the peritoneum and silk for the fascia, subcutaneous tissue and skin.

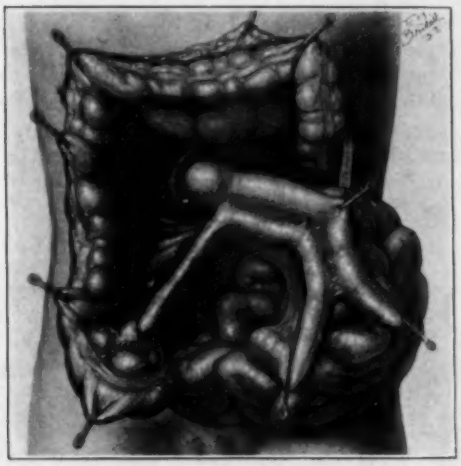

Fig. 13 (case 1).—Appearance after detorsion, showing the adhesions between the terminal ileum and the first part of the jejunum. The mesentery of these segments was also firmly adherent from the bowel to the attachment of the root of the mesentery to the posterior abdominal wall.

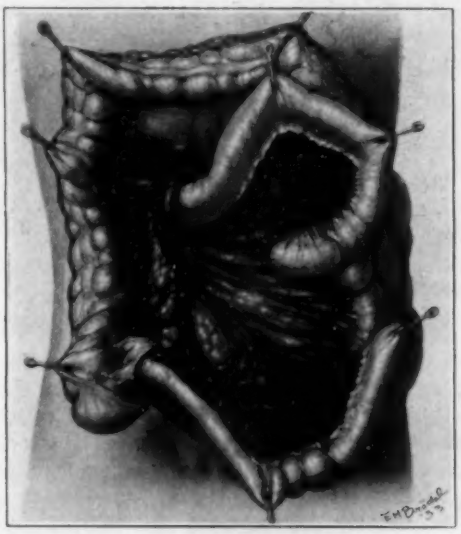

Fig. 14 (case 1).—Appearance at the end of operation. The two segments of bowel, with their mesenteries previously adherent, have been separated. The root of the mesentery is attached to the posterior abdominal wall over a distance of only about 3 cm. Enlarged veins, lymphatic vessels and lymph nodes in the mesentery of the midgut are shown. This enlargement is due to the long-standing partial obstruction of the veins and lymphatics at the point of the twist.

The postoperative convalescence was without event. Roentgen examination fifteen days after operation showed that the stomach and duodenum were still moderately dilated, but there was no gastric retention, and barium passed readily into the jejunum. The patient was discharged sixteen days after operation. A letter from the mother five months later reported that the child had been entirely relieved of all symptoms, that he ate anything he wished and weighed 41½ pounds (19 Kg.). The tonsils had been removed in February. The only unusual feature noticed by his mother was the occurrence of from three to five bowel movements a day.

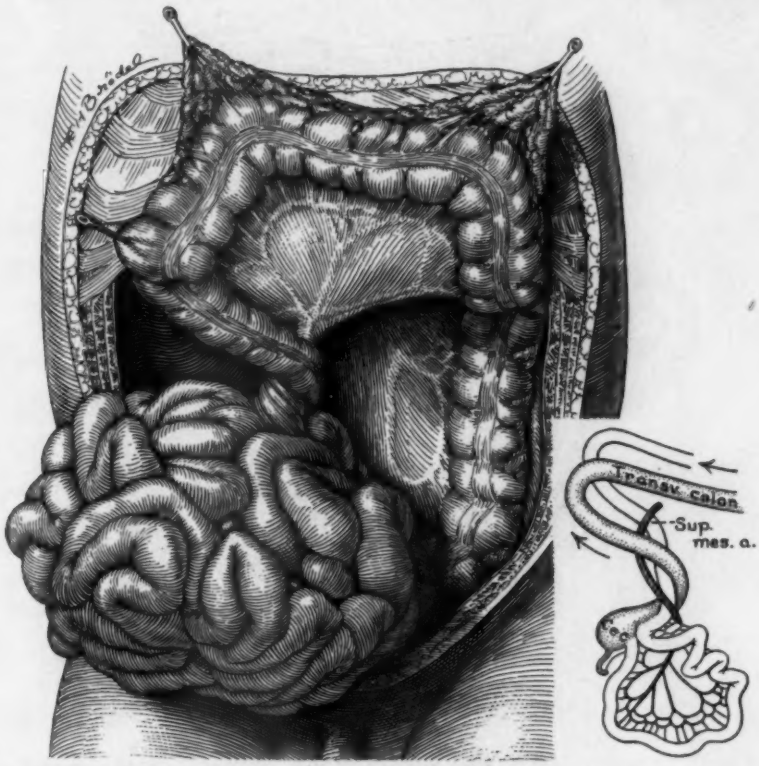

Fig. 15 (case 2).—Appearance on opening the abdomen (from a sketch made during operation). The hepatic flexure of the colon has become fixed normally; the cecum and ascending colon, however, remain suspended with the small intestine on a common mesentery. A 360 degree clockwise rotation of the entire small intestine, cecum and part of the ascending colon has taken place.

Case 2.—M. M., a colored boy, aged 2 months, was admitted to Duke Hospital in the pediatric service of Dr. W. C. Davison on Oct. 21, 1932, with a complaint of persistent vomiting for one month and pain and disability of the right arm for one week. The child, the first of apparently healthy parents, was born spontaneously at term, and weighed 7 pounds (3,175 Gm.) at birth. He had been normal in all respects until the age of 1 month when he began vomiting bile-stained material after one or two feedings each day. This had persisted until admission. The stools had remained normal, and there had been no loss of weight. In the

five days prior to entry pain and swelling of the right arm just above the elbow had developed, and the child had refused to use the arm.

The patient was a well developed, fairly well nourished male Negro infant of 2 months. He weighed 11 pounds (5.2 Kg.). There was no evidence of dehydration. The lower third of the upper part of the right arm was moderately and diffusely swollen, tender and indurated. The child did not use the right arm and resented motion at the elbow. The abdomen was full in the epigastric region. No peristalsis was seen, no tenderness elicited and no masses felt.

The hemoglobin was 45 per cent (Sahli); the red cell count was 3,110,000, and the white cell count, 10,400; the differential count was normal. The Schick, Dick

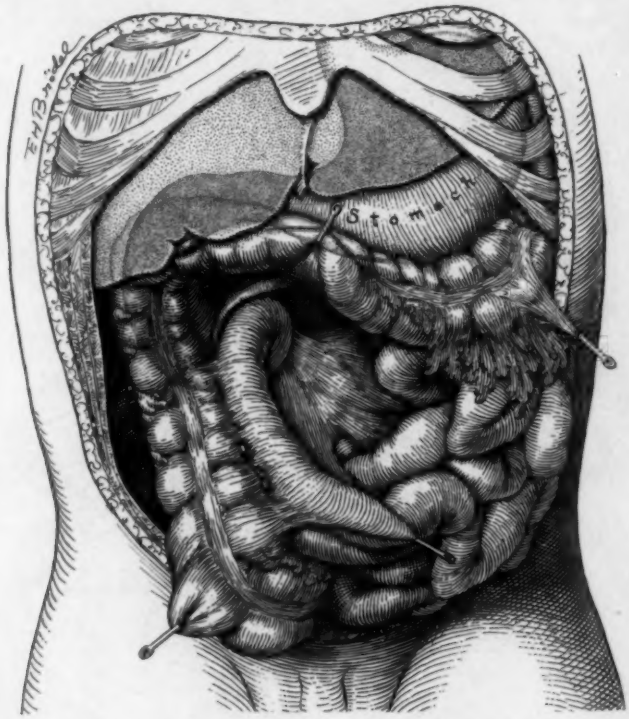

Fig. 16 (case 2).—Appearance after detorsion. The duodenum is dilated and entirely on the right of the midline. As in case 1 there are adhesions between the proximal and distal parts of intestine involved in the volvulus.

and tuberculin tests were negative. The Wassermann reaction of the blood was 4+. A roentgenogram of the right humerus showed a rarefaction and periostitis throughout the lower third with a fracture through the diaphysis.

Following a barium meal, obstruction in the third portion of the duodenum with dilatation of the duodneum and stomach was noted, and there was a small gastric retention after twenty hours. The colon was not filled at twenty hours. A barium enema showed an obstruction in the transverse colon.

During a ten day stay in the hospital the child vomited between 30 and 350 cc. of bile-stained material daily. The weight remained stationary. The lesion in the bone was considered as due to congenital syphilis, and the abdominal condition was diagnosed as volvulus of the entire midgut.

Operation was performed by one of us (D. H.) on Nov. 2, 1932. The abdomen was opened through a right rectus incision. A dilated stomach and duodenum immediately presented. The hepatic flexure of the colon was fixed in its normal position, and the ascending colon was seen to run from this point of fixation medially and downward until it disappeared in a twist around the root of the mesentery (fig. 15). It was immediately concluded that there was a volvulus of the intestinal tract from the duodenojejunal junction almost to the hepatic flexure of the colon. The rotated intestine was delivered. The twist was seen to be about

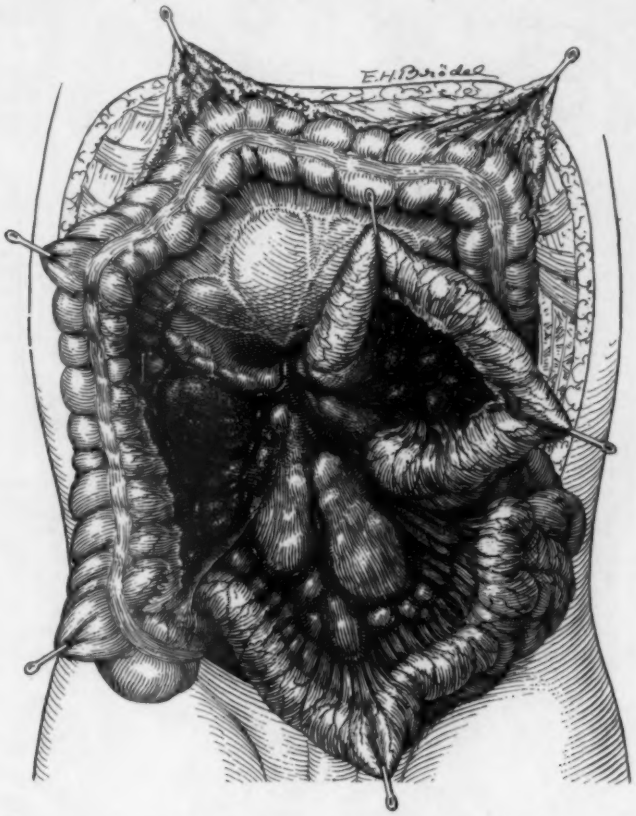

Fig. 17 (case 2).—Appearance after liberation of the adhesions. In the mesentery of the midgut there are dilated veins and lymphatics and enlarged lymph nodes as in case 1.

360 degrees in a clockwise direction. The veins and lymphatic vessels were dilated, though not as markedly as in case 1. The lymph glands were moderately enlarged. When the bowel was untwisted it was found that the cecum and lower part of the ascending colon were freely movable. The upper part of the ascending colon was adherent to the proximal part of the jejunum (fig. 16).

The two structures were dissected free, and the dissection was carried down between the mesenteries of each so that the cecum could be placed in the right lower quadrant and the proximal jejunum in the left upper quadrant (fig. 17). The small intestines were returned to the abdominal cavity so as to lie between

TABLE 1.—*Volvulus of the Entire Mesentery*

Case	Author	Year	Sex	Age	Symptoms and Signs	Bowel in Volvulus	Direction and Degree	Result
1	Kuljazbo and Koreski [22]...	1847	M	22	Attacks of abdominal colic, vomiting and diarrhea since childhood; present attack for 5 days; condition not recognized at operation; death on day of operation	Small intestine and ascending colon	4 turns	Death after operation
2	Bednar: Die Krankheiten der Neugebornen und Säuglinge, Vienna, C. Gerold, 1850, vol. 1, p. 127	1850	M	New-born	Normal bowel movements but persistent vomiting for 2 days before death; abdomen soft and not distended; death on ninth day	Small intestine and ascending colon	180 degrees clockwise	Death without operation
3	Leonard: Arch. gén. de méd. 1854, p. 242; quoted by Ekehorn, Arch. f. klin. Chir. **72**: 572, 1904	1854	M	20	Death after 9 days, suffering from ileus; no operation; at autopsy small intestine distended and filled with blood	Small intestine and ascending colon	360 degrees clockwise	Death without operation
4	Eppinger: Prag. Vrtljschr. f. pract. Heilk. **117**: 61, 1873	1873	F	New-born	No clinical history; death with autopsy on fourth day; small intestine, cecum and ascending colon on common mesentery	Small intestine	180 degrees clockwise	Death without operation
5	Whipham, T. T.: M. Times & Gaz. **2**: 33, 1876	1876	F	19	Similar attack 18 months previously; since then recurring attacks of abdominal cramps; seen on tenth day of illness with intestinal colic, vomiting of greenish material and obstipation; abdomen not distended; death on twelfth day; duodenum obstructed; bowel collapsed	Small intestine and ascending colon	Contra-clockwise	Death without operation
6	Firth, C.: Brit. M. J. **2**: 166, 1882	1882	M	49	Abrupt onset 5 days before entry with abdominal pain, vomiting and enlargement of hernia present for 5 years; fecal vomiting on admission; hernia easily reduced; condition not recognized at operation; death 3 days later; autopsy	Small intestine and ascending colon	540 degrees	Death after operation
7	Bruhns: St. Petersb. med. Wchnschr. **7**: 321, 1883	1883	M	24	Seen on fifth day of illness with symptoms of ileus; had had three previous similar attacks, the first 10 years previously; abdomen distended; peristaltic patterns visible; death 40 minutes after operation	Entire midgut	360 degrees clockwise	Death 40 minutes after operation with detorsion
8	Theremin, E.: Deutsche Ztschr. f. Chir. **8**: 34, 1877	1877	F	New-born	Vomiting of greenish material beginning on day after birth; abdomen somewhat distended; veins of epigastric region engorged; ineffectual enemas; death on third day	Small intestine and ascending colon	3½ turns clockwise	Death without operation
9	Theremin	1877	M	New-born	Vomiting of bile-stained material since birth; death on sixteenth day; autopsy	Small intestine and ascending colon	2 turns contra-clockwise	Death without operation
10	Soyka-Epstein: Prag. med. Wchnschr. **12**: 483, 1878	1878	..	New-born	Illness on fourth day with forceful and repeated vomiting and death on tenth day; at autopsy stomach and first part of duodenum tremendously distended	Small intestine and ascending colon	180 degrees clockwise	Death without operation
11	Brown, W. R.: Tr. Indian Branch Brit. M. A. **5**: 5, 1895; quoted by Vaughn, G. T.: Am. J. M. Sc. **75**: 799, 1903	1895	M	50	Operation 5 days after onset of colicky abdominal pain and constipation; abdomen distended; at operation, cecum on left side and small intestine distended	Small intestine	Contra-clockwise	Well after detorsion
12	Boyd, F. N.: Lancet **2**: 8, 1897	1897	F	39	For 6 years pain on eating relieved by vomiting; occasionally blood in stools and vomitus; ill 10 days with symptoms of ileus; abdomen distended; operation on tenth day, condition not recognized; autopsy	Small intestine and ascending colon	360 degrees contra-clockwise	Death after operation
13	Key, 1897, quoted by Brenner [43]	1897	M	Adult	Symptoms of ileus; operation on fourteenth day; condition not recognized; colostomy done; autopsy	Small intestine and ascending colon	360 degrees	Death after operation
14	Weinreich: Zentralbl. f. Chir. **51**: 986, 1898	1898	M	42	Sudden illness with symptoms of ileus; operation on eleventh day	Small intestine and ascending	220 degrees clockwise	Well after detorsion

					Symptoms of ileus; abdomen distended; operation on tenth day, condition not recognized; autopsy	colon	clockwise	
13	Key, 1897, quoted by Brenner [43]	1897	M	Adult	Symptoms of ileus; operation on fourteenth day; condition not recognized; colostomy done; autopsy	Small intestine and ascending colon	360 degrees	Death after operation
14	Weinreich: Zentralbl. f. Chir. **51**: 986, 1898	1898	M	42	Sudden illness with symptoms of ileus; operation on eleventh day	Small intestine and ascending colon	220 degrees clockwise	Well after detorsion
15	Helmsmuller [32]	1898	M	20	Sudden onset after violent jump; severe abdominal pains; collapse; death after 6 hours; at autopsy bloody peritoneal fluid and intestine filled with blood	Entire midgut	360 degrees contra-clockwise	Death without operation
16	Schreiber, E.: Ztschr. f. klin. Med. **38**: 426, 1899	1899	M	9	Repeated attacks of abdominal pain, vomiting and constipation since birth; death on fifth day of attack; vomitus voluminous greenish material, never fecal; abdomen moderately distended; at autopsy stomach and duodenum tremendously distended	Small intestine and ascending colon	360 degrees contra-clockwise	Death without operation
17	von Manteuffel, L.: Samml. klin. Vortr. no. 260, 1899, p. 1421	1899	M	20	After lifting sack of grain, cramping abdominal pain with vomiting of bile-stained material and constipation; no abdominal distention; operation on sixth day; death 3 days later	Small intestine and ascending colon	90 degrees clockwise	Death after operation
18	Hausmann [30]	1900	M	22	Four similar previous attacks; operation on fifth day of intestinal obstruction; reversed rotation with common ileocecal mesentery; kink at hepatic flexure straightened allowing feces to pass; death on following day; at autopsy, postoperative volvulus of entire small intestine with cecum in region of spleen; position of cecum normal at first operation	Small intestine	180 degrees contra-clockwise	Death after operation
19	Durante [33]	1901	..	Newborn	Persistent vomiting since birth; vomitus contained some blood; blood passed per rectum; death on third day	Entire midgut	450 degrees clockwise	Death without operation
20	Frölich: Bull. et mém. Soc. de chir. de Paris **27**: 542, 1901	1901	M	3	Abdominal pain, vomiting, constipation and distention for 15 days; condition not recognized at operation; death in 36 hours; autopsy	Entire midgut	Contra-clockwise	Death after operation
21	Blecher [26]	1902	M	25	Sudden onset of abdominal pain with collapse and vomiting of bile-stained material; no distention; death during operation 12 hours after onset; bloody peritoneal fluid, blood in intestine	Small intestine and ascending colon	360 degrees contra-clockwise	Death during operation
22	Burgess, A. H.: Lancet **2**: 1690, 1902	1902	M	8	Sudden onset, acute abdominal pain with vomiting of greenish material, no distention; collapse; death 16 hours after onset	Small intestine and ascending colon	360 degrees clockwise	Death without operation
23	Krogius-Faltin: Nord. med. ark. **2**: 89, 1903	1903	F	24	Recurring attacks of abdominal pains for several years; operation after 4 days of abdominal colic, vomiting and constipation; death on fifth day	Small intestine and ascending colon	1½ turns clockwise	Death after operation
24	Wandel: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **11**: 54, 1903	1903	M	7	Periodic attacks of abdominal pain, vomiting and constipation since birth; similar attack 6 days after fracture of left femur; vomitus bile-stained; abdomen not distended; death on fourteenth day; duodenum obstructed	Small intestine and ascending colon	360 degrees clockwise	Death without operation
25	Pescatore, M.: Deutsche Ztschr. f. chir. **68**: 185, 1903	1903	M	Newborn	No clinical history given; autopsy on nineteenth day; duodenum enormously distended	Small intestine and ascending colon	1½ turns clockwise	Death without operation
26	Ekehorn, G.: Arch. f. klin. Chir. **72**: 572, 1904	1904	F	15	Illness for 3 weeks with abdominal pain and vomiting; abdomen distended, vomitus fecal; death 10 hours after detorsion and resection of gangrenous cecum and ascending colon	Small intestine and ascending colon	360 degrees clockwise	Death after operation

TABLE 1.—*Volvulus of the Entire Mesentery—Continued*

Case	Author	Year	Sex	Age	Symptoms and Signs	Bowel in Volvulus	Direction and Degree	Result
27	Möhring: Deutsche med. Wchnschr. **1**: 162, 1905	1905	F	72	Recurring attacks of abdominal pain with constipation for 1 year; recently frequent vomiting; abdomen distended; fecal material in stomach; operation; bloody peritoneal fluid	Small intestine and ascending colon	180 degrees clockwise	Well after detorsion
28	Danielson, W. and Kuttner: Beitr. z. klin. Chir. **48**: 100, 1906	1906	F	55	Abdominal pain, vomiting and constipation for 4 days; abdomen distended; peristalsis present; death from peritonitis 9 days after operation	Small intestine and ascending colon	360 degrees clockwise	Death after detorsion
29	Clément, P.: Ann. de gynec. et d'obst. **3**: 567, 1906	1906	..	Newborn	Child normal at birth; took feedings well and passed meconium; on second day abdomen and veins of abdominal wall became distended; death on second day of illness	Entire midgut	2 turns clockwise	Death without operation
30	Müller, E.: Zentralbl. f. allg. Path. u. path. Anat. **20**: 514, 1909	1909	M	Newborn	Death with autopsy on fifth day; no clinical history given	Small intestine and ascending colon	360 degrees clockwise	Death without operation
31	Müller	1909	F	15	Frequent attacks of abdominal cramps with vomiting since age of 2; death in collapse during an attack; autopsy, common ileocecal mesentery	Small intestine	2 turns clockwise	Death without operation
32	Billington, W.: Lancet **1**: 678, 1909	1909	M	41	Attacks of abdominal cramps with vomiting lasting 2 or 3 days every 8 or 9 months for 4 years; seen on sixth day of attack; abdomen moderately distended; swelling in left upper quadrant later found to be caused by enormously distended cecum; operation on sixth day	Small intestine and ascending colon	Not given	Well after detorsion
33	Blecher: Deutsche Ztschr. f. Chir. **98**: 521, 1909	1909	M	20	Several previous attacks of abdominal pain and vomiting; operation on second day of an attack; vomiting of bile-stained material containing a worm; two stools of bright blood; abdomen not distended; preoperative diagnosis, mesenteric thrombosis or intussusception	Small intestine and ascending colon	180 degrees contra-clockwise	Well after detorsion
34	Hubner [9]	1910	M	3	Attacks of abdominal colic with vomiting at 4 to 8 week intervals; seen in an attack; abdomen moderately distended; cysts palpable in epigastrium and lower left quadrant; at operation mesenteric cyst and 6 cm. of small bowel resected; death on following day; autopsy showed volvulus of midgut	Entire midgut	360 degrees	Death after operation
35	Michaelis [28]	1913	M	Newborn	Normal delivery; passed meconium; on second day went into collapse, passed blood in stool; death on following day	Small intestine and ascending colon	1½ turns contra-clockwise	Death without operation
36	Weible, R. E.: Surg, Gynec. & Obst. **19**: 644, 1914	1914	M	27	Attacks of colic and abdominal distention all his life; seen on third day of an attack; had had diarrhea for first 2 days; enemas ineffectual on third day; vomited dark material; moderate distention; common ileocecal mesentery	Small intestine	180 degrees clockwise	Well after detorsion
37	Eschbach, quoted by Weible: Surg., Gynec. & Obst. **19**: 644, 1914	1914	M	Newborn	Death with autopsy on eighth day; no clinical history given	Entire midgut	Clockwise	Death without operation
38	Köhler [33]	1918	F	23	Sudden onset of severe abdominal pain while at work; no vomiting; seen after 2 hours in collapse; pulse imperceptible; abdomen distended; immediate operation with diagnosis of ruptured ectopic pregnancy; blood-tinged abdominal fluid; intestines filled with blood; vomited	Small intestine and ascending colon	360 degrees contra-clockwise	Death after detorsion

	Obst. **19**: 644, 1914			born	given			operation
38	Köhler [32]	1918	F	23	Sudden onset of severe abdominal pain while at work; no vomiting; seen after 2 hours in collapse; pulse imperceptible; abdomen distended; immediate operation with diagnosis of ruptured ectopic pregnancy; blood-tinged abdominal fluid; intestines filled with blood; vomited blood after operation	Small intestine and ascending colon	360 degrees contra-clockwise	Death after detorsion
39	Ombredanne, L.: Bull. et mém. Soc. de chir. de Paris **45**: 688, 1919	1919	F	11	Since age of 18 months repeated frequent attacks of vomiting; daily vomiting of large amounts of bile-stained material for 2 months before operation; dehydration, emaciation; gastric tetany; no distention; roentgen rays showed duodenal obstruction	Entire midgut	1½ turns clockwise	Well after detorsion and colopexy
40	Rixford [31]	1920	M	5	Recurring attacks of colic and vomiting since birth; never had been able to take a full meal without initiating an attack; emaciation; unable to be up more than a few hours a day because of weakness; abdomen distended in epigastrium, scaphoid below	Entire midgut	360 degrees clockwise	Well after detorsion
41	Kotzareff, A.: Bull. et mém. Soc. nat. de chir. **46**: 577, 1920	1920	M	12	No clinical history given; autopsy showed obstruction to third part of duodenum; also abnormality of mesenteric arteries	Entire midgut	3 turns clockwise	Death after operation
42	Hamann [21]	1922	M	23	Recurring attacks of colic and vomiting since birth; operation for acute appendicitis; cecum mobile but on right side; on fifth day, intestinal obstruction; death on ninth; at autopsy, cecum on left side; duodenum obstructed	Entire midgut	180 degrees contra-clockwise	Death without operation
43	Eggers, C.: Ann. Surg. **75**: 757, 1922	1922	F	30	Intermittent attacks of abdominal pain without vomiting for 10 years; seen on second day of attack; abdomen distended; operation; patient also had large hydrops of appendix	Entire midgut	180 degrees clockwise	Well after detorsion
44	Heyman [44]	1922	M	31	Recurring attacks of abdominal pain and vomiting for 6 years, aggravated by taking food; emaciation; gastric retention on roentgen examination; at operation, cecum adherent in Treitz fossa with 180 degree clockwise volvulus of small intestine and ascending colon; also duodenal ulcer; Billroth I resection of stomach, detorsion and colopexy	Small intestine and ascending colon	180 degrees clockwise	Well after detorsion and colopexy
45	Heyman [44]	1922	M	20	Malaise and indefinite abdominal pain for 6 months; sudden attack, severe epigastric pain 3 weeks before; nausea, anorexia and constipation since then; roentgen examination showed duodenal obstruction; operation; cecum adherent to duodenum with resolving abscess of appendix behind duodenum	Small intestine and ascending colon	180 degrees clockwise	Well after detorsion and colopexy
46	Dott [4]	1923	M	Newborn	Normal for 5 days; then vomiting after feedings; vomitus green colored; stools normal for 5 days, then a little blood noticed in one stool; vomiting regularly 20 minutes after feeding; no distention; gastric peristalsis visible on seventh day of illness; operation; obstruction at duodenum; death after 12 hours	Entire midgut	450 degrees clockwise	Death after gastrojejunostomy
47	Dott [4]	1923	F	Newborn	Normal for 3 days, then began vomiting after feeding; vomitus soon bile-stained and on third day contained a little blood; passed meconium per rectum but never normal stool; upper part of abdomen distended and gastric peristalsis visible; emaciated and dehydrated; operation; obstruction at duodenum; death after 7 hours; autopsy showed malrotation and deficient fixation of midgut	Small intestine	360 degrees clockwise	Death after gastro-enterostomy

TABLE 1.—*Volvulus of the Entire Mesentery—Continued*

Case	Author	Year	Sex	Age	Symptoms and Signs	Bowel in Volvulus	Direction and Degree	Result
48	Braeunig [12]	1924	M	21	Previously healthy; operation after 3 hours of symptoms of acute strangulation; ileus; found reversed rotation with volvulus of entire small intestine, cecum and ascending colon; obstruction at hepatic flexure	Small intestine and ascending colon	360 degrees clockwise	Death after resection of cecum and ascending colon
49	Poynton, F. J.: Lancet **1**: 1045, 1924	1924	F	3	Recurring attacks of vomiting and abdominal pain aggravated by meals since age of 1 month; attacks at intervals of from 6 to 8 weeks lasting 3 or 4 days; seen on fifth day of an attack, vomiting feculent material; abdominal pain and obstipation; passed an offensive stool on sixth day; no abdominal distention; death on eighth day; autopsy showed common ileocecal mesentery	Small intestine	360 degrees clockwise	Death without operation
50	Poynton	1924	M	3½	Attacks of abdominal pain and vomiting at age of 5 and 7 months; seen on fourth day of attack; abdominal pain, vomiting of thick greenish material and obstipation; no abdominal distention; death on eighth day; at autopsy common ileocecal mesentery with cecum in region of spleen	Small intestine	1½ turns clockwise	Death without operation
51	Poynton	1924	M	12	Recurring attacks of abdominal pain and vomiting for 2½ years; autopsy after death in an attack	Small intestine	2 turns contra-clockwise	Death without operation
52	Wheeler, J. B.: Boston M. & S. J. **190**: 230, 1924	1924	F	8	Repeated attacks of vomiting and abdominal pain since birth; admitted on second day of attack with vomiting of greenish material, abdominal pain and obstipation; no abdominal distention; at operation bowel collapsed; long mesentery	Small intestine	1½ turns clockwise	Well after detorsion
53	Baker, A. H., and Mizen, V.: Brit. M. J. **1**: 1031, 1926	1926	M	Newborn	Normal for 6 days; then vomiting 20 to 30 minutes after feedings; vomitus bile-stained on second day; stools normal at first, then contained only greenish mucus; visible gastric peristalsis on fifth day; lower abdomen scaphoid; death on tenth day	Entire midgut	180 degrees clockwise	Death without operation
54	Schöttle, A.: Deutsche Ztschr. f. Chir. **194**: 401 1926	1926	F	23	Attacks of abdominal pain and constipation for 3 years; for preceding 6 weeks vomiting and abdominal colic after meals; roentgen examination showed duodenal obstruction with 20 per cent gastric retention in 4 hours; operation	Entire midgut	360 degrees clockwise	Well after detorsion
55	Schöttle	1926	F	30	Pain in lower part of abdomen; belching and constipation for 2 weeks, more severe for 2 days; abdomen moderately distended, tender in its lower half; operation for appendicitis; ascaris passed in stools after operation	Small intestine and ascending colon	180 degrees clockwise	Well after detorsion and cecopexy
56	Valkanyi, R.: Paris méd. **1**: 95 (Jan. 23) 1926	1926	..	Newborn	Premature birth (eighth month); normal for 1 week; on eighth day, after a bath, vomiting, obstipation and distention; operation, death next day; autopsy showed common ileocecal mesentery	Small intestine	Not given	Death after detorsion
57	Lawson [27]	1927	M	40	For 4 years frequent attacks of abdominal pain and vomiting; admitted moribund on fifth day of an attack; had passed pinkish fluid by rectum on the fourth day; at necropsy, dorsal attachment of mesentery 1 inch (2.54 cm.) in length	Small intestine	720 degrees contra-clockwise	Death without operation
58	Spencer, F. M.: Brit. M. J. **1**: 1005, 1927	1927	M	Newborn	Normal delivery; passed meconium; on second day refused to nurse, seemed in pain; abdomen slightly distended; no stool; operation on second day, death 4 hours later	Small intestine	360 degrees clockwise	Death after operation
59	Dickerson [28]	1927	M	New-	Normal delivery; on second day, vomiting of dark green	Entire midgut	360 degrees	Well after

					had passed pinkish fluid by rectum on the fourth day; at necropsy, dorsal attachment of mesentery 1 inch (2.54 cm.) in length		contra-clockwise	operation
58	Spencer, F. M.: Brit. M. J. **1**: 1005, 1927	1927	M	Newborn	Normal delivery; passed meconium; on second day refused to nurse, seemed in pain; abdomen slightly distended; no stool; operation on second day, death 4 hours later	Small intestine	360 degrees clockwise	Death after operation
59	Pinkerton [25]	1927	M	Newborn	Normal delivery; on second day, vomiting of dark green material; thereafter vomiting from 20 to 30 minutes after feedings; seen at age of 4 weeks; passing blood by rectum in quantities; roentgen examination showed duodenal occlusion; operation on twenty-fifth day	Entire midgut	360 degrees clockwise	Well after detorsion
60	Donald [19]	1927	F	27	Epileptic, 5 months pregnant; an attack of intestinal colic 2 years previously; typical signs and symptoms of intestinal obstruction of 24 hours' duration; operation; reversed rotation with volvulus of small intestine and ascending colon	Small intestine and ascending colon	2½ turns clockwise	Death after cecostomy
61	Dott [29a]	1927	F	Newborn	Normal birth; passed meconium; on fourth day suddenly seemed in abdominal pain; vomitus at first clear, then bile-stained; obstipation; blood-stained mucus passed per rectum on eighth day; dehydration; distention of upper part of abdomen; at operation common ileocecal mesentery; duodenum obstructed by root of mesentery; small bowel collapsed	Small intestine	360 degrees clockwise	Well after detorsion
62	Oberling [24]	1927	..	Newborn	Seen (moribund) on fifth day; history of having vomited everything taken by mouth since birth; vomitus blood-stained; autopsy, bloody peritoneal fluid, duodenum compressed by root of mesentery	Small intestine and ascending colon	360 degrees contra-clockwise	Death without operation
63	Oberling [24]	1927	..	Newborn	Death on ninth day; no clinical history	Small intestine and ascending colon	3 turns clockwise	Death without operation
64	Oberling [24]	1927	M	12	Frequent attacks of vomiting since birth; death in collapse during an attack; at autopsy duodenum tremendously dilated	Entire midgut	360 degrees contra-clockwise	Death without operation
65	Lusena, G.: Arch. ital. di chir. **21**: 428, 1928	1928	M	11	Periodic attacks of abdominal pain every 20 to 30 days since birth; attacks aggravated by solid foods; roentgen examination showed left-sided colon; at operation cecum and ascending colon fixed in left hypochondrium; common ileocecal mesentery	Small intestine	360 degrees contra-clockwise	Well after detorsion and colopexy
66	Radaeli [18]	1928	F	45	Primipara in ninth month of pregnancy previously without symptoms; complained suddenly of violent abdominal pain; vomiting, collapse; death 22 hours after cesarean section; volvulus not recognized at operation; autopsy	Small intestine and ascending colon	180 degrees clockwise	Death after cesarean section
67	Lust, M. and Bourg, R.: Bruxelles-méd. **9**: 219, 1928	1928	M	Newborn	Normal until second day; passed meconium; projectile vomiting of bile-stained material beginning on second day until death on seventh day; superficial abdominal veins dilated	Entire midgut	180 degrees contra-clockwise	Death without operation
68	Charsley and Richardson [30]	1928	M	Newborn	Vomiting green fluid since birth; dark bowel movements which on third day became fluid blood; blood leaked constantly from rectum in quantity; abdomen soft; epigastrium distended; death on sixth day; at autopsy blood-stained peritoneal fluid; root of mesentery very short; bowel gangrenous	Small intestine	Contra-clockwise	Death without operation
69	Schram-Andersen, J.: Rev. franç. de pédiat. **5**: 622, 1929	1929	F	9 mos.	Repeated attacks of vomiting of bile-stained material; abdominal distention since birth; roentgen examination showed gastric retention and left-sided colon; death 18 hours after operation	Small intestine and ascending colon	180 degrees clockwise	Death after detorsion

TABLE 1.—*Volvulus of the Entire Mesentery—Continued*

Case	Author	Year	Sex	Age	Symptoms and Signs	Bowel in Volvulus	Direction and Degree	Result
70	Mole, R. H.: Brit. J. Surg. **17**: 670, 1930	1930	F	8	Attacks of epigastric pain, vomiting and malaise of 3 to 7 days' duration every 4 to 6 months since birth; final attack of 7 days' duration with copious vomiting of bile-stained material and obstipation; at autopsy, duodenum obstructed	Entire midgut	180 degrees contra-clockwise	Death without operation
71	Skinner, A. H.: China M. J. **44**: 53, 1930	1930	M	Newborn	History of vomiting since birth; had passed meconium; upper abdomen distended; operation on second day; condition not recognized; at autopsy, root of mesentery only three fingerbreadths in length	Small intestine	180 degrees clockwise	Death after operation
72	Moulonguet, Doleris and d'Aubigne: Bull. et mém. Soc. de chir. de Paris **56**: 122, 1930	1930	M	21	Since age of 11, intermittent attacks of vomiting; patient emaciated, dehydrated; recent persistent vomiting of bile; at first operation detorsion of volvulus; returned at request after 4 months for cecopexy	Small intestine and ascending colon	180 degrees clockwise	Well after detorsion
73	Moulonguet, Doleris and d'Aubigne	1930	M	55	Colicky abdominal pain of 24 hours' duration; no vomiting; moderate distention; operation	Small intestine and ascending colon	360 degrees clockwise	Death after detorsion and cecopexy
74	Haymond and Dragstedt [5]	1931	M	16	Since birth intermittent attacks of vomiting at intervals of from 1 to 4 weeks; vomitus bile-stained; attacks aggravated by heavy meals; roentgen examination showed a duodenal obstruction with 33 per cent gastric retention in 5 hours; at operation, cecum in left hypochondrium and common ileocecal mesentery	Small intestine	120 degrees clockwise	Well after detorsion
75	Green, T. M.: Surg., Gynec. & Obst. **53**: 734, 1931	1931	F	Newborn	Projectile vomiting of all feedings and large quantities of bile since birth; roentgen examination showed duodenal obstruction; operation on tenth day	Entire midgut	1½ turns clockwise	Well after detorsion and fixation
76	Green	1931	F	Newborn	Projectile vomiting of all feedings and large quantities of bile since birth; visible gastric peristalsis; operation on fourth day with diagnosis of volvulus of the midgut; adhesions between duodenum and cecum	Small intestine	1¾ turns clockwise	Well after detorsion and fixation
77	Brenner [42]	1932	F	30	Constipation all of her life; attack of abdominal colic 1 year previously; seen after 30 hours of colicky abdominal pain and vomiting; abdomen tremendously distended; visible intestinal peristalsis; operation with detorsion of volvulus of entire midgut; recovery; recurrence of symptoms of acute intestinal obstruction 9 months later; operation after 10 hours; exactly similar condition found as at first operation; well after detorsion and fixation	Entire midgut	360 degrees clockwise	Well after second operation with detorsion and fixation
78	Brenner [42]	1932	F	26	Sudden onset; colicky abdominal pain with vomiting, obstipation and abdominal distention 36 hours previously; abdomen tremendously dilated; operation; proximal half of colon tremendously dilated	Entire midgut	180 degrees clockwise	Well after detorsion and fixation
79	Lee [42]	1932	M	11	Recurring attacks of colicky abdominal pain and vomiting from 4 to 7 days every month since early infancy; roentgen examination showed obstruction in duodenum and left-sided colon; at operation veins in ascending mesocolon tremendously dilated	Small intestine	180 degrees clockwise	Well after duodenojejunostomy and ileocolostomy
80	Benham [14]	1932	M	29	Inmate of sanatorium; cerebral diplegia since age of 15;	Small intestine and ascending	180 degrees contra-	Death after operation

80	Benham [14]	1932	M	29	Inmate of sanatorium; cerebral diplegia since age of 15; sudden onset of abdominal pain and vomiting; collapse after 10 hours; operation; entire intestinal tract gangrenous	Small intestine and ascending colon	180 degrees contra-clockwise	Death after operation
81	Moritz [15]	1932	M	Newborn	Vomiting and constipation since birth; roentgen examination showed duodenal obstruction; operation in third week	Small intestine and ascending colon	360 degrees clockwise	Death after operation
82	Moritz [15]	1932	M	Newborn	Vomiting since birth; roentgen examination showed duodenal obstruction; operation at seventh week; volvulus so adherent detorsion not thought possible	Small intestine and ascending colon	360 degrees clockwise	Death after operation
83	Ladd [36]	1932	M	Newborn	Projectile vomiting of bile-stained material beginning on eleventh day; visible gastric peristalsis; roentgen examination showed duodenal obstruction; operation on fourteenth day; common ileocecal mesentery	Small intestine	Not given	Well after detorsion
84	Ladd [36]	1932	M	9 mos.	Intermittent vomiting since birth; operation at ninth month with detorsion of volvulus of entire small intestine; common ileocecal mesentery; recurrence of symptoms after 1 month; second operation, detorsion, mobilization of cecum from adhesions in lower left quadrant; recovery	Small intestine	Not given	Well after second detorsion
85	Ladd [36]	1932	F	Newborn	Vomiting of bile-stained material since birth; visible gastric peristalsis; operation at 4½ weeks; duodenum obstructed	Entire midgut	180 degrees clockwise	Well after detorsion
86	Helms, J. S.: J. Florida M. A. **18**: 265, 1931	1931	M	35	Periodic attacks of nausea and vomiting between ages of 6 and 14; similar symptoms in past 2 years; roentgen examination showed tremendous dilatation of duodenum; at operation, common ileocecal mesentery	Small intestine	180 degrees	Well after detorsion and duodeno-jejunostomy
87	Gardner and Hart	1933	M	6	Repeated periodic attacks of abdominal cramps and vomiting of bile since third day after birth; dehydration; malnutrition; abdomen flat; roentgen examination showed duodenum dilated and on right side of vertebral column	Small intestine	360 degrees clockwise	Well after detorsion
88	Gardner and Hart	1933	M	2 mos.	Vomiting of bile for 1 month; congenital syphilis with involvement of lower part of right humerus; roentgen examination showed duodenal obstruction with gastric retention for 20 hours	Small intestine and ascending colon	360 degrees clockwise	Well after detorsion

TABLE 2.—*Reversed Rotation with Obstruction of the Colon by Torsion or Kinking*

Case	Author	Year	Sex	Age	Symptoms and Signs	Result
1	Tscherning, E.: Nord. med. ark. **15**: 1, 1883	1883	M	56	Death with autopsy on nineteenth day of illness with symptoms of intestinal obstruction	Death without operation
2	Clairmont, P.: Arch. f. klin. Chir. **76**: 316, 1905	1905	M	48	Abdominal pain with vomiting for 3 years; diagnosis of duodenal ulcer with obstruction to pylorus; at operation, duodenal ulcer found and anterior gastro-enterostomy performed; death 8 days later with signs of ileus; autopsy	Death without operation
3	Strehl, H.: Arch. f. klin. Chir. **87**: 8, 1908	1908	F	12	Previously healthy; seen on eighth day of illness with lower abdominal cramps and vomiting; abdomen distended; operation; death after 8 hours	Death after cecostomy
4	Hunter [10]	1922	..	Newborn	Breech delivery at term; did not take feedings well; seemed in constant abdominal pain; bowels kept open with frequent enemas; death on seventh day; at autopsy, reversed rotation and mesenteric cyst of jejunal origin	Death without operation
5	Dott [4]	1923	M	68	Acute intestinal obstruction of 3 days' duration; similar attack 10 years previously; abdomen distended; outline of distended ascending colon visible, extending from upper right to lower left quadrant; at operation, reversed rotation with 180 degrees clockwise torsion of ascending colon; gangrenous patches in ascending colon; death 3 days after operation	Death after resection of right half of colon
6	Harvey [25]	1926	F	Newborn	Vomiting of greenish material and no bowel movements since birth; abdomen distended, especially on right side; operation on third day; gangrenous patches with perforation of ascending colon	Death after operation
7	Walker, H. B.: Edinburgh M. J. **33**: 725, 1926	1926	M	28	Acute intestinal obstruction of 24 hours' duration; at operation, adhesion across upper part of abdomen released; actual condition only recognized at autopsy 3 days later; dextrocardia diagnosed clinically; autopsy limited to abdomen	Death after operation; condition not recognized
8	Serck-Hanssen [45]	1926	F	21	Attacks of indigestion with vomiting for 1 year; seen in an attack; abdomen distended; enemas ineffectual; at operation, reversed rotation with volvulus of the mobile cecum	Well after detorsion and fixation of cecum
9	Lee [42]	1929	M	24	Repeated attacks of abdominal colic as a boy; last attack 4 years previously; seen on fourth day of an attack; no vomiting since first day; abdomen distended, especially in right lower quadrant; at operation last two loops of ileum with cecum and ascending colon in reversed position; death 24 hours after evacuating cecum and replacing it through the orifice	Death after operation
10	Peigneaux and Fruchard [34].....	1930	F	15	Premature child; repeated attacks of vomiting and abdominal colic since birth; operation during an attack; found reversed rotation with partial obstruction at duodenum and transverse colon	Recovery after anterior gastro-enterostomy and lateral transverse colocolostomy

TABLE 3.—*Duodenal Obstruction from Abnormal Intestinal Fixation*

Case	Author	Year	Sex	Age	Symptoms and Signs	Result

TABLE 3.—*Duodenal Obstruction from Abnormal Intestinal Fixation*

Case	Author	Year	Sex	Age	Symptoms and Signs	Result
1	Foisy, E.: Bull. et mém. Soc. de chir. de Paris **45**: 1548, 1919	1919	F	14	Since age of 3 weeks, periodic attacks of vomiting of bile-stained material with epigastric pain; recently, epigastric pain after all meals; weak and malnourished; at operation, duodenum distended, fixed in kink on right side of vertebral column; common ileocecal mesentery with partial torsion of ascending colon	Well after release of kink in duodenum and colopexy
2	Denzer [37]	1922	..	Newborn	Delivery by cesarean section because of toxemia of pregnancy in eighth month; vomited all food since birth; death on twenty-sixth day; vomitus had been persistent and bile-stained; stools at first yellow, then watery and green; abdomen scaphoid; at autopsy, nonrotation, obstruction of duodenum caused by sharp duodenojejunal angle and squeezing of duodenum between ileum and cecum which was firmly bound down to posterior peritoneum at level of Treitz fossa	Death without operation
3	Thompson, J. W.: Brit. J. Surg. **16**: 332, 1928	1928	F	23	Since age of 18; pain after eating; vomiting so that now able to retain only small quantities of food; at operation, nonrotation with duodenum obstructed by a kink at junction of first and second parts; transverse colon with long loop hanging into the pelvis	Well after duodenostomy, colocolostomy and cecocolopexy
4	Grant, J. W. G.: Surg., Gynec. & Obst. **46**: 133, 1928	1928	F	57	For many years, fulness and flatulence following meals; for 6 weeks, persistent vomiting so that little or no food could be retained; at operation, nonrotation; duodenum obstructed by a double S-shaped kink firmly adherent to posterior abdominal wall; death after 3 days	Death after duodenojejunostomy
5	Ladd [36]	1932	F	Newborn	Premature infant; onset 17 hours after birth; vomiting; persistent bile-stained vomitus since then; fulness in upper part of abdomen with visible peristalsis; lower part of abdomen scaphoid; roentgen examination showed markedly dilated duodenum; operation at age of 2 weeks; cecum fixed on left with obstruction of third portion of duodenum; death after 53 hours	Death after duodenojejunostomy
6	Ladd [36]	1932	F	11	Abdominal cramps and vomiting for 2 weeks; jaundice after fourth day; vomitus bile-stained; abdomen not distended at onset; before operation, epigastric distention and visible peristalsis; at operation, duodenum dilated to half the size of the stomach, obstructed by a nonrotated cecum firmly attached to the posterior abdominal wall over it	Well after cecum was freed from attachment across duodenum
7	Ladd [36]	1932	M	2	Seen first at 4½ months with history of intermittent attacks of biliary vomiting for 1 month; epigastrium distended with visible peristalsis; barium enema showed nonrotation; seen 2 years later; had had periodic attacks of vomiting of bile-stained material; undernourished; dehydrated; upper part of abdomen distended; at operation, duodenum dilated; cecum in left upper part of abdomen with transverse colon crossing duodenum	Well after duodenum was freed

these structures and hold them in their normal position. The abdominal incision was closed in layers, catgut being used for the peritoneum and silk for the sheath of the rectus, subcutaneous tissues and skin.

Postoperative convalescence was uneventful. The patient remained in the hospital under an active antisyphilitic regimen until December 30, and since then has reported irregularly at the clinic for similar treatment. He has been completely relieved of all digestive disturbances. On April 7, 1933, roentgen examination after the barium meal showed that the stomach emptied rapidly. There was no dilatation of the duodenum, and barium passed through it without delay. A barium enema showed that the entire colon filled and lay in the normal position.

COMMENT

In both cases the clinical history and the physical findings were characteristic of a chronic duodenal obstruction. In both cases operation revealed a volvulus of the entire mesentery. The intestine was obstructed at the duodenojejunal junction, at which point the emerging segment of bowel looped around the entering segment and the twisted root of the mesentery. In each the emerging loop of bowel was not obstructed and the small bowel was collapsed. In both cases chronicity of symptoms, density of adhesions binding together entering and emerging segments of bowel and evidences of long-standing venous and lymphatic obstruction make it seem probable that the volvulus had been present since intra-uterine life or occurred shortly after birth. In case 1 normal rotation and fixation of the colon had taken place, though the duodenum remained on the right side of the vertebral column and the attachment of the root of the mesentery was inadequate. It is possible that volvulus took place during the process of reduction of the midgut loop in the tenth week of uterine life and that the colon subsequently rotated normally. It is more probable, however, that the deficient fixation of the mesenteric root predisposed to volvulus which was produced by the vigorous intestinal peristalsis incident to the first feedings. In case 2, the condition was exactly similar except that the cecum and ascending colon were also involved; deficient fixation of the common mesentery permitted formation of the volvulus. It is possible that the volvulus occurred at the age of 1 month; however, the evidences of long standing venous and lymphatic engorgement in the mesenteries of the midgut and the density of adhesions binding together the two loops of bowel involved in the twist suggest the possibility that the volvulus had been present since early intra-uterine life.

CASES IN WHICH ANOMALIES OF INTESTINAL ROTATION LED TO OBSTRUCTION OF THE INTESTINAL TRACT

Anomalies of intestinal rotation may exist without symptoms and be recognized only at anatomic dissection, at necropsy, on roentgen examination after a barium meal or incidentally at operation. Symptoms

appeared in only 13 of Dott's 48 cases collected in 1923. Incident to the present collection of 105 cases [7] with varying degrees of intestinal obstruction we have collected 70 cases of major defects in intestinal rotation which existed without symptoms. The first of these was reported in 1827 by Cruveilhier.[8]

Intestinal obstruction, either acute or chronic, may develop on the basis of anomalies of intestinal rotation because of (1) volvulus of the entire mesentery, (2) kinking or torsion of the ascending colon secondary to reversed rotation of the midgut loop or (3) kinking or pressure on the intestinal tract from abnormal fixation of the mesentery. In this report we have not included the cases with symptoms from an unduly mobile cecum or those of volvulus of the cecum, conditions which are undoubtedly secondary to a defect in the third stage of intestinal rotation but about which there is no confusion in the literature.

Age and Sex.—Of the 105 cases 55, or 52 per cent, were reported in new-born infants or in patients in whom symptoms had dated from a few days after birth. The latter group ranged in age from a few months to 27 years. Of the other 49 cases in which the age was given, 21 occurred in the third decade and from 3 to 7 in each of the other first six decades. Sixty-two per cent of the 97 patients whose sex was indicated were males.

Etiology.—Any departure from the orderly sequence of return of the intestine from the umbilical hernia into the abdomen is the reason given by Dott [4] for abnormalities of rotation. He believes that an unduly large umbilical orifice would exert no particular restraining influence on the cecum and thus permit a disorderly reduction. In cases of abnormal intestinal rotation reported by Hubner,[9] Hunter [10] and Reinhold [11] mesenteric cysts were also present, and it is quite possible that their presence in fetal life acted as obstructions to normal intestinal reduction. In the other cases no apparent cause for the anomaly could be found. The presence of other congenital anomalies has been noted

7. These cases comprise 103 collected from the literature and the 2 cases reported here.

8. Cruveilhier, E.: Disposition particulière de péritoine. Duodenum pourvu d'un mésentère; mésentère unique pour tous les intestins, Bull. Soc. anat. de Paris **2**:202, 1827.

9. Hubner, Hans: Volvulus des gesamten Dünndarmes und aufsteigenden nebst einem Teile des queren Dickdarms beim Mesenterium ileocolicum commune nach Exstirpation einer Mesenterialzyste, Virchows Arch. f. path. Anat. **201**:427, 1910.

10. Hunter, J. I.: A Mesenteric Cyst of Jejeunal Origin Complicated by Retrojejeunal Position of the Transverse Colon, Brit. M. J. **2**:800, 1922.

11. Reinhold, Paul: Kyste du mésentère compliqué de volvulus du grêle et du colon. Resection du kyste et de l'intestin grêle. Reduction du volvulus. Guérison, Bull. et mém. Soc. de chir. de Paris **58**:523, 1932.

by Braeunig [12] whose patient also had a Meckel's diverticulum, by Grant [13] whose patient had a congenital absence of the shaft of the left radius, left thumb and first metacarpal, by Benham [14] whose patient had congenital cerebral diplegia, by Moritz [15] whose patient was a cretin, by Sauerbeck [16] whose patient had a patent interventricular septum and by Sencert [17] whose patient had an imperforate anus.

Contributory causes for the development of volvulus have been attributed to violent physical exertion, blows on the abdomen, exposure to extremes of temperature, operative manipulation, tumors, adhesions, starvation, constipation, vigorous cathartics and overeating. Any of these factors may have a bearing on the production of perversions in intestinal peristalsis which are probably most often the cause of the development of a volvulus. In volvulus neonatorum, of which there were 55 cases in this series, symptoms dated from the first few days of life and were probably initiated by the peristaltic efforts of the intestinal tract incident to the first food taken. In 2 cases (Radaeli [18] and Donald [19]) volvulus of the entire mesentery complicated pregnancy, while in 3 cases (Hubner,[9] Hausmann [20] and Hamann [21]) it occurred as a postoperative complication.

Volvulus of the Entire Mesentery.—This is the most common cause of intestinal obstruction secondary to anomalies of intestinal rotation and accounted for 88, or 83 per cent, of the 105 cases. If the condition of nonrotation and absence of intestinal fixation is present the suspension of the entire midgut from the narrow pedicle at the origin of the superior mesenteric artery may permit the development of a volvulus

12. Braeunig, Karl: Volvulus des Dünndarms und Colon ascendens bei Hemmungsmissbildung des Darms, Deutsche Ztschr. f. Chir. **186**:284, 1924.

13. Grant, J. W. G.: Case of Non-Rotation of the Intestine, Brit. J. Surg. **18**:166, 1930.

14. Benham, H. W.: An Unusual Case of Volvulus, Lancet **2**:340, 1932.

15. Moritz, A. R.: Mesenterium Commune with Intestinal Obstruction, Am. J. Path. **8**:735, 1932.

16. Sauerbeck, Ernst: Ueber Entwickelungshemmung des Mesenteriums und abnorme Lageverhältnisse des Darms, insbesondere des Dickdarms, Arch. f. klin. Chir. **89**:873, 1909.

17. Sencert: Cas d'arrêt de torsion de l'intestin, Compt. rend. Soc. de biol. **58**:325, 1905.

18. Radaeli, Guilio: Sopra un caso di ileo in gravidanza da volvulo del tenue, del cieco e del colon ascendente, Ann. di ostet. e ginec. **50**:1085, 1928.

19. Donald, Charles: Volvulus of Small Gut, Caecum and Ascending Colon Associated with Congenital Reversed Rotation of Intestine and with Pregnancy, Brit. J. Surg. **15**:269, 1927.

20. Hausmann, L.: Beiträge zu den Lageanomalien des Darmes: Mesenterium Commune, Postposition des Dickdarms (Col. Transversum) hinter dem Dünndarms (Duodenum) Achsendrehung, Zentralbl. f. Chir. **27**:19, 1900.

21. Hamann, C. A.: Faulty Rotation of the Intestine, Ann. Surg. **76**:491, 1922.

of the entire small intestine, cecum and ascending and right half of the transverse colon. Such a volvulus of the entire midgut was present in 23 of the 88 cases of total volvulus. On the other hand, the presence of malrotation or of nonrotation with deficient fixation may predispose to formation of a volvulus of the entire small intestine, such as occurred in 24 of the 88 cases, or of the entire small intestine, cecum and ascending colon, such as occurred in 41 of the cases.

Two degrees of volvulus of the entire mesentery may be recognized pathologically depending on the tightness of the torsion and on the degree of vascular occlusion. If the twist obstructs both the entering and the emerging segment of bowel and the blood supply is obstructed, the entire involved intestine becomes enormously distended and gangrenous. The pathologic picture in such a condition is the usual one of acute intestinal obstruction with strangulation. On the other hand, if the volvulus is less tight, as is more frequently the case, the third part of the duodenum is obstructed at the point where it winds around the mesenteric root, while the colon, which is less fixed, is not occluded. Since the involved bowel has a free exit below through the colon it remains collapsed, while the stomach and duodenum become enormously distended. The picture is thus entirely one of duodenal obstruction without any of the usual features of volvulus. If the vascular occlusion is acute there may be a bloody peritoneal fluid, and blood may be extravasated into the bowel and subsequently passed by rectum. If the volvulus is chronic, as in both of our cases, evidences of long-standing venous and lymphatic obstruction will be apparent. In such a case the mesentery of the midgut will be thickened, and in it may be found enlarged lymph nodes, dilated lymphatic vessels and veins as large as one's finger.

The direction of rotation was clockwise in 56, or 70 per cent, of the 79 cases of volvulus in which it was indicated. Torsions varying from 120 degrees to four complete turns were encountered. Tightness of the torsion rather than the number of turns determines the severity of the symptoms. Benham's case [14] was seen in collapse ten hours after the onset of symptoms with a torsion of 180 degrees while in the case of Kuljazbo and Koreski,[22] operation was performed on the fifth day of symptoms, and four complete turns of the mesentery were found.

Clinically two entirely different forms of volvulus of the entire mesentery may be encountered. In the one the picture is entirely that of acute or chronic obstruction to the duodenum without any of the usual signs of volvulus. In the other the picture is typical of volvulus with acute intestinal obstruction with or without evidence of strangulation.

22. Kuljazbo and Koreski, quoted by Brenner.[43]

Volvulus with Symptoms of Duodenal Occlusion.—This is the more common condition which follows volvulus of the entire intestinal tract and was present in 52 (70 per cent) of the 75 cases in which the description was complete enough for analysis. The obstruction may be partial, complete or intermittent. Usually symptoms are chronic, frequently beginning within a few days after birth and consist of recurring attacks of abdominal pain, vomiting and constipation without abdominal distention.

This condition has been reported in 32 new-born infants. No intestinal abnormality is apparent at birth. The first feedings are taken normally. Meconium and in some cases normal stools are passed. Vomiting, constipation and abdominal pain usually manifest themselves about the third or fourth day. Vomiting is persistent and projectile. It occurs usually from twenty to thirty minutes after feedings (later than in congenital pyloric stenosis) and in cases reported by Dott,[4] Durante [23] and Oberling [24] the vomitus contained blood. Since the obstruction is below the ampulla in the duodenum, the vomitus always contains bile. Epigastric distention and frequently visible gastric peristalsis are present, while the lower part of the abdomen remains scaphoid. If vascular obstruction accompanies the volvulus, blood-stained fluid may be passed by rectum as in cases reported by Pinkerton,[25] Blecher,[26] Durante,[23] Lawson,[27] Michaelis [28] and Dott [29] (2 cases). In the case of Charlsey and Richardson [30] blood leaked continuously and in large quantity from the rectum. Acidosis, dehydration and demineralization of the blood may be extreme and may cause the child's death. In cases in which the volvulus has progressed to complete strangulation death occurs much more promptly and is probably hastened by the rapid loss of blood into the intestinal tract.

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23. Durante, G.: Occlusions congénitales de l'intestin, Bull. Soc. anat. de Paris **6**:593, 1901.

24. Oberling, Charles: Trois cas de volvulus par torsion du mésentère commun persistant, Rev. franç. de pédiat. **3**:96, 1927.

25. Pinkerton, C. C.: Volvulus Neonatorum Due to Anomalous Intestinal Rotation, Ann. Surg. **86**:633, 1927.

26. Blecher: Ueber Ileus bedingt durch seltenere Formen von Volvulus, Deutsche Ztschr. f. Chir. **64**:48, 1902.

27. Lawson, T. C.: Volvulus of the Entire Small Intestine, California & West. Med. **26**:189, 1927.

28. Michaelis, P.: Achsendrehung des Dünndarms und des Colon ascendens bei einem Neugeborenen, Wien. klin. Rundschau **27**:662, 1913.

29. (*a*) Dott, N. M.: Volvulus Neonatorum, Brit. M. J. **1**:230, 1927; (*b*) footnote 4.

30. Charlsey, G. W., and Richardson, G.: A Case of Volvulus Neonatorum, Brit. M. J. **1**:494, 1928.

If the condition is less acute the child may escape death in early infancy but will remain susceptible to repeated attacks of partial duodenal obstruction throughout the remainder of his life. Seventeen such cases in an age group of from 3 to 27 years are included in this series. These patients had a history, dating from birth, of repeated attacks of abdominal pain, vomiting and constipation but without abdominal distention. The pain is usually the typical cramp of intestinal colic, though it may manifest itself only as an epigastric discomfort. It is frequently precipitated by meals and usually relieved by vomiting. Vomiting is forceful and copious; the vomitus is bile-stained and frequently contains food residue of meals eaten many hours previously. The upper part of the abdomen is distended; the lower, scaphoid, and visible gastric peristalsis may be evident during attacks. Constipation is generally present although occasionally small stools of normal fecal material are passed during attacks. Blood in the vomitus or in the stools did not occur in any of the cases. Pathetic degrees of emaciation and dehydration often occur. Rixford [31] reports the case of a child aged 5 years who had never been able to eat a full meal without initating an attack. Because of the weakness of starvation this patient could be out of bed only a few hours each day.

Roentgen examination of the gastro-intestinal tract reveals a partial obstruction in the duodenum, usually in the third portion, with enlargement of the duodenum and stomach and prolonged retention of barium in these organs (fig. 11). The characteristic finding, however, and the one on which the roentgenologist may frequently establish a diagnosis of an anomaly in intestinal rotation, is the presence of the entire duodenum on the right side of the vertebral column. The normal curve of the duodenum to the left across the midline and under the stomach is lost. This condition was present in case 1. The visualization of the colon entirely on the left side of the abdomen is indicative of an abnormality of rotation. However, in these cases sufficient barium to fill the colon satisfactorily rarely passes the duodenal obstruction. The entire colon, if not involved in the volvulus, will be filled by a barium enema, and "left-sided colon," if present, is easily detected. At other times, as in case 2, there may be an obstruction to the passage of barium by an enema beyond the site of the volvulus in the right half of the colon.

Volvulus with Symptoms of Acute Intestinal Obstruction.—This condition was present in 23 of the cases of total volvulus. The symptomatology is not unlike that of acute intestinal obstruction from any cause. except that the vomitus is rarely fecal. The usual picture is that of

31. Rixford, E.: Failure of Primary Rotation of the Intestine (Left-Sided Colon) in Relation to Intestinal Obstruction, Ann. Surg. **72**:114, 1920.

sudden onset of acute intestinal colic with vomiting, obstipation and abdominal distention. Symptoms of strangulation with death in collapse as early as six hours after the onset may be present (Helmsmuller [32]). In Köhler's [33] case seen in collapse two hours after onset the condition was mistaken for a ruptured ectopic pregnancy. A history of one or two similar attacks in a milder form is sometimes given; usually, however, these patients have enjoyed excellent health and have been singularly free from abdominal discomfort. It is probable that before operation this condition cannot be distinguished from any other form of acute intestinal obstruction.

Reversed Rotation with Acute Obstruction of the Colon.—In reversed rotation the transverse colon comes to lie under the duodenum and superior mesenteric artery and may become trapped in this position by the acquired atttachment of the root of the mesentery (fig. 10). Obstruction to the transverse colon at the point where it pierces the root of the mesentery may take place by torsion or kinking of the mobile cecum and ascending colon. Thirteen cases of reversed rotation have been collected. In 3 (Hausmann,[20] Braeunig [12] and Donald [19]) attachment of the mesenteric root was inadequate, and volvulus of the entire mesentery took place. In the other 10 cases (table 2) obstruction occurred in the middle of the transverse colon secondary to kinking or torsion of the right half of the colon which retained its primitive mesentery.

Symptoms of this condition are not unlike those of acute obstruction of the colon from any cause. Frequently a history of repeated milder attacks in the past may be elicited, or the condition may exist without symptoms for years, as in the case of Dott [4] whose patient, 68 years of age, was seen in his second attack. Peigneaux and Fruchard [34] reported the case of a 15 year old girl with an associated chronic duodenal obstruction, symptoms of which had been present since birth. In the cases of Hunter [10] and Harvey [35] the condition caused death in the new-born. On abdominal examination the outline of the tremendously dilated cecum and ascending colon may be made out. It is improbable that before operation this condition can be distinguished from any other type of acute obstruction of the colon. However,

32. Helmsmuller: Ein Fall von Achsendrehung des gesamten Dünndarms und des aufsteigenden Dickdarms, Thesis, Kiel, 1898; quoted by Blecher.[26]

33. Köhler, H.: Volvulus des Zokokolons und des gesamten Dünndarms, Deutsche med. Wchnschr. **44**:519, 1918.

34. Peigneaux, and Fruchard, Henri: Troubles digestifs graves chez une jeune fille de quinze ans en relation avec des malformations portant sur le duodenum et le colon droit, Bull. et mém. Soc. de chir. de Paris **56**:335, 1930.

35. Harvey, Frank: Intestinal Obstruction in a Child of Three Days Due to Abnormal Intestinal Rotation, Brit. J. Surg. **14**:187, 1926.

should it be encountered at laparotomy, a knowledge of the possibility of such a condition is of great value.

Obstruction from Abnormal Intestinal Fixation.—Seven cases of obstruction of the duodenum caused by abnormal fixation of the intestinal tract incident to anomalies of intestinal rotation have been collected (table 3). In 5, fixation of the duodenum in abnormal kinks caused the obstruction. In Ladd's [36] case the duodenum was occluded by the firm fixation of a nonrotated and abnormally fixed cecum across it, while in Denzer's [37] case the duodenum was tightly squeezed between the nonrotated and abnormally fixed cecum and the terminal ileum.

In addition to these 7 cases of duodenal obstruction Woolsey [38] reported 2 cases with symptoms of indigestion and flatulence in which the nonrotated cecum was firmly fixed to the gallbladder, pylorus and duodenum. These symptoms were probably caused by dysfunction of the gallbladder rather than by duodenal obstruction. Brouet and Caroli [39] reported the case of a boy aged 17 who had had frequent attacks of abdominal pain and in whom at operation nonrotation of the midgut with adhesions between the ascending colon and the right loop of the transverse colon were found. Recovery followed right colectomy and ileocolostomy. Hecker [40] reported the case of a woman aged 52 who for a year had suffered from recurring abdominal pains and in whom at operation nonrotation with adhesions between the colon and the small intestine were found. In 1927 Waugh [41] reported 5 cases in which malformation of the mesentery accounted for a variety of abdominal symptoms; in 1930 Grant [13] reported the case of a man aged 32 who had had recurring attacks of abdominal pain and in whom nonrotation of the midgut loop without volvulus or abnormal fixation was found.

Symptoms and clinical findings in the patients with duodenal occlusion secondary to abnormal intestinal fixation are the same in every respect as those of duodenal obstruction from volvulus. In the second group with symptoms due to unusual position and fixation of the intestines Waugh [41] emphasized the "unusualness" of the pain, the

36. Ladd, W. E.: Congenital Obstructions of the Duodenum in Children, New England J. Med. **206**:277, 1932.

37. Denzer, B. S.: Congenital Duodenal Obstruction; Malrotation of the Intestine, Am. J. Dis. Child. **24**:534 (Dec.) 1922.

38. Woolsey, R. A.: Non-Rotation of the Midgut, Internat. J. Med. & Surg. **40**:314, 1927.

39. Brouet, and Caroli: Arrêt de torsion de l'intestin, Bull. et mém. Soc. de chir. de Paris **54**:366, 1930.

40. Hecker, Paul; Grünwald, E., and Kuhlmann, C. J.: Les anomalies congénitales de forme et de position du gros intestin et leur importance chirurgicale, Rev. de chir., Paris **64**:661, 1926.

41. Waugh, George E.: Congenital Malformations of the Mesentery: A Clinical Entity, Brit. J. Surg. **15**:438, 1927.

"emptiness" of the right iliac fossa as a result of the absence of the cecum from its normal position, and the roentgen findings after the barium meal as the important factors which enabled him to make the correct preoperative diagnosis in 4 of his 5 cases.

Diagnosis.—It is improbable that a correct preoperative diagnosis of volvulus of the entire mesentery causing acute intestinal obstruction or reversed rotation with acute obstruction to the colon can be made unless an anomaly of intestinal rotation has been previously recognized in the patient. However, the condition should be recognized before operation in new-born infants, children and young adults who show symptoms of acute or chronic duodenal obstruction without evidence of volvulus. The differential diagnosis is to be made from hypertrophic pyloric stenosis, congenital atresia or stenosis of the intestine, intussusception, volvulus of a limited portion of the intestine, or intestinal obstruction from tumors or from anomalous intraperitoneal bands.

The persistent vomiting following feedings, the epigastric distention and the visible gastric peristalsis in the new-born may cause a confusion in diagnosis with pyloric stenosis. In total volvulus, however, the vomiting is always bile-stained as the obstruction is below the ampulla of Vater; symptoms usually begin earlier in life, and the vomiting occurs at a longer interval after feedings. Congenital atresia of the duodenum may be distinguished by the fact that in this condition vomiting begins immediately after birth and meconium is not passed by rectum. Congenital stenosis of the lower duodenum in which the obstruction is partial closely simulates the partial duodenal obstruction of total volvulus. In the former condition symptoms date from birth, while in the latter they date only from the onset of the volvulus. Roentgenologic findings of a duodenum wholly on the right of the vertebral column is the greatest aid in differentiating the two conditions. In congenital stenosis of the intestine and in the acquired intestinal obstructions from tumors, peritoneal bands, intussusception and volvulus of a limited segment of the intestine, differentiating features are found in the generalized abdominal distention and in the vomitus which soon becomes feculent. These symptoms are present in all the latter conditions but not in the duodenal obstruction resulting from volvulus of the entire mesentery.

Treatment.—Operative treatment offers the only hope of cure in patients with obstruction to the duodenum or lower intestinal tract secondary to anomalies of intestinal rotation. In the group with symptoms of acute intestinal obstruction, whether in the duodenum or lower, early operation is imperative, for in these cases as in any acute intestinal obstruction the mortality rate mounts rapidly with each hour of delay. In the group with chronic duodenal obstruction with intermittent acute attacks a more leisurely preparation for operation may be

pursued. However, in this group nonoperative treatment is not justified, as evidenced by the fact that in our series 8 of the 17 patients with this condition died without operation during acute exacerbations of the attacks from which they had suffered all their lives.

Volvulus of the entire mesentery may be easily overlooked at operation if the condition is not kept in mind or if adequate exploration is not made. The condition may be suspected if the right half of the colon is not found in its normal position or if on palpation a firm cord representing the twisted root of the mesentery can be felt at the site of origin of the superior mesenteric artery. Adequate exposure with visualization of this area usually makes the diagnosis obvious, although evisceration may be necessary before the condition becomes clear. Detorsion of the volvulus after complete evisceration of the involved intestine with replacement of the viscera in their normal position is the ideal operative procedure. Duodenojejunostomy alone has been performed successfully in one case (Lee [42]). Because of the vascular and lymphatic obstruction which inevitably accompanies volvulus and because of the possibility that this obstruction may become complete we do not consider this procedure advisable. If, after detorsion, the condition of the patient permits, some form of fixation of the cecum and ascending colon in their normal position is advisable. In cases reported by Ladd [36] and Brenner [43] recurrence of the volvulus occurred one and nine months, respectively, after the original operation in which simple detorsion had been performed. In each case this necessitated a second operation with detorsion and fixation of the ascending colon. In the 2 cases reported by Heyman [44] a tendency for the volvulus to recur while the abdomen remained open was noted, and in each colopexy was found necessary to maintain reduction of the volvulus. If adhesions bind together entering and emerging loops of bowel involved in the volvulus, as occurred in both of our cases, these adhesions must be carefully and thoroughly freed before reduction can be maintained. It is probable that the secondary adhesions which form about the raw surfaces thus produced will prevent recurrence of the volvulus, and on such an assumption colopexy was not performed in either of our cases. In the 30 patients with total volvulus who survived operation the procedure was as follows: simple detorsion, 19; detorsion and fixation of the cecum and ascending colon, 9; duodenojejunostomy, 1, and detorsion and duodenojejunostomy, 1.

42. Lee, A. E., and Nye, L. J. J.: Chronic Duodenal Obstruction Due to Non-Rotation of the Midgut Loop with Superadded Volvulus, M. J. Australia **2**:18, 1932.

43. Brenner, E. C.: Total Volvulus, Am. J. Surg. **16**:34, 1932.

44. Heyman, E.: Volvulus des gesamten Dünndarms, Deutsche med. Wchnschr. **48**:725, 1922.

Acute obstruction to the colon secondary to reversed rotation may be recognized at operation by the enormous dilatation of the mobile cecum and ascending colon, the distention ending abruptly at the point where the transverse colon passes under the duodenum. In our series only 2 of the 10 patients with this condition survived. One of these was treated by reduction of the kink in the colon and cecopexy (Serck-Hanssen [45]); the other, by lateral colocolostomy (Peigneaux and Fruchard [34]); complete relief of symptoms occurred in both cases. Either of these forms of treatment may be applied in the early cases, but in obstructions of long duration a temporary cecostomy after untwisting of the mobile cecum is probably the procedure of choice. This relieves the acute obstruction and also fixes the cecum in normal position so as to prevent a recurrence. In such condition it is impossible to replace the colon in its normal position.

In the case of duodenal obstruction caused by abnormal intestinal fixation, release of the obstruction by freeing the duodenum from its attachment to the parietal peritoneum is the procedure of choice. Duodenojejunostomy may be performed as an alternative. Of the 4 patients with this condition who survived operation 1 had had a duodenojejunostomy, while the other 3 had had simple release of the abnormal duodenal attachment.

Prognosis.—The prognosis in obstruction to the intestinal tract subsequent to anomalies of rotation depends on the level, the degree of obstruction, the presence or absence of strangulation and the time of operation after the onset of symptoms. All the patients not operated on died. Of the 32 patients with volvulus neonatorum reported within the first months of life 16 died without operation, and of the 16 operated on 8, or 50 per cent, recovered. Of the 17 patients in an age group between 3 and 27 years with volvulus and with symptoms of duodenal obstruction dating from birth, 8 died without operation during acute exacerbation of their attacks. Eight, or 88 per cent, of the 9 operated on survived and were cured. Of the 39 adults in whom the condition occurred, 8 died without operation, and of the remaining 31 operated on 14, or 45 per cent, recovered. In the group of 88 cases of volvulus of the entire mesentery 32 patients died without operation, and of 56 subjected to operation 30, or 53 per cent, survived and were cured. Three of the 10 patients with reversed rotation and obstruction of the colon died without operation and only 2, or 28 per cent of the 7 operated on, survived. Of the 7 patients with duodenal obstruction caused by abnormal intestinal fixation 1 died without operation and 4, or 66 per cent, of the 6 operated on survived and were cured. In the entire series

45. Serck-Hanssen, Trygne: Retroposition Coli, Volvulus Coeci, Med. Rev., Bergen **43**:557, 1926.

of 105 cases 36 patients died without operation, while 36, or 52 per cent, of the 69 subjected to operation survived and were relieved of all symptoms.

SUMMARY

1. A precise knowledge of the possibilities of derangement of the intestinal tract incident to anomalies of intestinal rotation is essential.

2. The stages in normal intestinal rotation and the possibilities of abnormality in each are described.

3. Two cases of volvulus of the entire mesentery secondary to abnormalities of intestinal rotation with symptoms of chronic duodenal obstruction seen by us are presented in detail.

4. One hundred and five cases of intestinal obstruction incident to abnormalities of intestinal rotation are collected from the literature. Eighty-eight of these were caused by volvulus of the entire mesentery, 10 by obstruction to the transverse colon secondary to reversed rotation and 7 by obstruction of the duodenum by abnormal intestinal fixation.

5. Symptoms of acute intestinal obstruction may accompany volvulus of the entire mesentery. More often the picture is that of acute, chronic or intermittent obstruction of the duodenum below the ampulla without any of the usual evidences of volvulus.

6. Correct preoperative diagnosis of the cases causing duodenal obstruction should be made.

7. Operative treatment for each form of obstruction is considered.

GENERAL SENSATIONS IN PEDUNCULATED FLAPS OF SKIN

JOHN STAIGE DAVIS, M.D.
AND
EDWARD A. KITLOWSKI, M.D.
BALTIMORE

The fact that the sensations of touch, pain and temperature eventually return in skin grafts and in pedunculated flaps of skin [1] and subcutaneous tissue after transplantation has been known to surgeons for a long time, but so far as we are able to ascertain, no attempt has been made to find out what the early sensations are in pedunculated flaps and what relationship these sensations have to each other.

Several years ago, we began to gather from our clinical work in plastic surgery data which could eventually be analyzed and from which we hoped to obtain definite information as to these points. A large amount of material has been accumulated, and from this we have selected small groups of flaps of different types, which are typical and which indicate the results obtained.

It will be noted that the observations listed in this report deal entirely with pedunculated flaps and are largely for the purpose of determining the early relationship of the sensations of touch, pain and temperature. The majority of the observations were made quite early on flaps in which the transfer was delayed, such as tubed flaps, while other observations were made on flaps which were immediately transferred to fill the defect for which they were prepared. However, in some tubed flaps it was possible to make observations months after they were formed but still before their transplantation.

The regeneration of sensations in skin grafts and in transplanted flaps in which the pedicles have been divided has been considered in another report.[2]

Since the work of Head and his associates [2a] the subject of the general sensations in the skin has received much attention, and controversies have arisen about the relationship of the sensations to each other after

1. A flap of skin is an area of skin and subcutaneous tissue attached at some portion of its periphery or base by a pedicle or pedicles, through which it receives its blood supply and which can be shifted only so far as the pedicle allows.

2. Davis, John Staige, and Kitlowski, E. A.: Regeneration of Nerves in Skin Grafts and Skin Flaps, Am. J. Surg. **24**:501 (May) 1934.

2a. Head, Henry, and others: Studies in Neurology, New York, Oxford University Press, 1920, vol. 1.

nerves have been cut and sutured. Trotter and Davies,[3] Boring[4] and Cobb[5] question the disassociation theory of Head and believe that the region of sensory loss is approximately the same for all forms of sensibility. The whole subject has been ably summarized by Lee[6] in his report "The Regeneration of Nervous Tissue." Like Trotter and Davies and Boring, we have secured results similar to Head, using the same methods, which all agree are very satisfactory clinically. A brief explanation of the different types of sensibilities, as postulated by Head and his associates and by Lickley,[7] is as follows:

Epicritic sensibility refers to the finely graded and definitely localized sensations of tactile impressions and mild degrees of heat and cold. This sensibility exists in the skin only.

Protopathic sensibility refers to the sensations of pain and extreme degrees of heat and cold. This sensibility is the more primitive, existing in the skin and in the viscera, and acts as a defensive agency against pathologic changes in the tissues.

A third system of general sensations existing at the periphery, known as the deep set, arising from the muscles, joints, etc., conveys the sensibilities of position, deep pressure and pain and movements in the muscles, joints and tendons.

These sensations may be stimulated in groups or individually, depending on the type and intensity of the stimuli. A very light touch which does not depress the skin or disturb the hair on the skin is reported by the epicritic system. If the touch is pressure which causes a depression in the surface of the skin, it is reported by the epicritic system which definitely localizes it and also by the deep system reporting pressure. If the pressure is more severe, causing pain, it is reported by the epicritic system which localizes the spot and by the deep system which reports pain. If the epicritic system is eliminated by some cause, the pressure is reported as coming grossly from a certain region, but without accurate localization of the exact area. If there is gentle touch only and the epicritic system is not functioning, there will be no consciousness of touch.

The sensation of pain as elicited by the prick of a sharp pointed instrument, as a needle or pin, is reported by the protopathic system.

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3. Trotter, W., and Davies, H. M.: Experimental Studies in the Innervation of the Skin, J. Physiol. **38**:134, 1909.

4. Boring, E. G.: Cutaneous Sensation After Nerve Divisions, Quart. J. Exper. Physiol. **10**:1, 1916.

5. Cobb, S.: Cutaneous Sensibility in Cases of Peripheral Nerve Injury, Arch. Neurol. & Psychiat. **2**:505 (Nov.) 1919.

6. Lee, F. C.: The Regeneration of Nervous Tissue, Physiol. Rev. **9**:575 (Oct.) 1929.

7. Lickley, J. D.: The Nervous System, New York, Longmans, Green & Co., 1931.

The epicritic system accurately localizes the point because the stimulus arouses this system when it touches the skin before causing pain. The deep system is also brought into action by the pressure of the instrument, and if the stimulus is very severe that system also reports pain. Absence of the epicritic system causes pain to be reported in a general region without accurate information about the exact area. If both the epicritic and the protopathic systems are not functioning the prick is reported as pressure unless the stimulus is very intense, when it is recognized as pain. This stimulus must, however, be so intense as to injure tissue before it is recognized. Thus an area lacking the epicritic and protopathic sensations can be incised, the patient feeling pressure only.

METHODS OF TESTING

In view of the difficulties necessarily encountered in testing the flaps, we determined to limit our investigations to sensations of touch, pain and temperature. In order to test for both the epicritic and the protopathic systems as defined by Head and others,[2] we limited our test of touch to epicritic touch and used the prick test to elicit pain as an expression of the protopathic system. The tests of temperature were made with extremes of heat and cold and are an expression of the protopathic system.

Before beginning the tests every effort was made to obtain the cooperation and interest of the patient. All the patients, as will be noted in the time after operation in which the test was performed, had recently undergone some more or less unpleasant operative experience, and it was necessary to assure them that these tests would not cause further pain or be distressing to them in any way. The tests were carefully explained and demonstrated in full view of the patient so that each one would understand what was desired. The patient was then placed in the most comfortable position possible and asked to report with a simple "yes" or "no" concerning the sensation. The tests were carried out in a quiet room, and the patient was not permitted to observe the actions of the operator, so that the replies would not be influenced by what was seen. If a patient showed a tendency to tire or to permit his attention to wander, the test was stopped and resumed after a short period of rest. The tests were made by one of us (E. A. K.) in order to eliminate any difference in personal error.

Light touch was tested by the use of a bit of cotton wrapped around the end of a toothpick and frayed so that wisps of the cotton alone touched the skin. The sensation of touch can be elicited in several ways: by touching the skin, by pressing on the skin and by touching the hairs of the skin. Any pressure, however slight, which causes a depression in the surface of the skin, produces a sensation of touch which is reported through the protopathic system. A more intense pressure elicits an additional response from the system of deep sensibility located in the tissues underlying the skin. Touch is also reported by sensory nerve organs at the bases of hairs, believed to belong to the protopathic system, which are stimulated by any movement of the hairs. The sensation of light touch not conveyed by pressure or movement of the hairs is a finer tactile impression which is carried by the epicritic system. It was this light touch which we tested. The wisps of cotton were applied

gently to the skin, and the patient was asked to report whether he felt them or not. As a rule the areas used for securing flaps were not hairy and, in addition, had been shaved before operation so that the hairs were not a factor in our tests. Inasmuch as we were interested in the gross data only, tests with von Frey[8] hairs were not used. The wisps of cotton were gently applied to the skin until a point was reached at which the patient did not feel the touch. This point was then marked with 5 per cent solution of brilliant green in alcohol applied with the point of a toothpick. The process was repeated until the whole flap had been tested. The points were then joined, and the line so formed indicated the limit of the sensation of touch.

Sensibility to pain was tested by pricking the skin with a sharp pointed pin or needle. The patient was first instructed to distinguish between prick and touch. No effort was made in these tests to determine the intensity of the pain, and we were careful to make sure that the patient could distinguish between sharpness and soreness. The pressure applied was so slight that the sensation of pain which is elicited by pressure was not produced in our tests. The skin was pricked gently over the entire area, and the points at which pain was no longer felt were marked. This procedure was repeated a number of times over the same part to make sure that no pain spot was missed.

The sensibility to heat and cold was tested by means of ordinary test tubes containing cracked ice or hot water. This method is useful in securing only the coarsest observations since it is impossible to record the exact temperature as the glass will be of a different temperature from the contents when it comes in contact with the skin. The extremes of temperature gave information about the protopathic system. We did not test with moderate degrees of heat or cold, sensations which are conveyed by the epicritic system. The test tubes were placed on the skin and moved from spot to spot until the patient did not feel either heat or cold. The test was performed first with the cold and then with the hot tube. We did not attempt to separate the two sensations in our tracings. The end of a test tube is rather large, so that the findings could not be very accurate, and we simply noted their location in regard to the limits of the sensations of light touch and pain.

After the sensations had been tested and their limits marked, a piece of perforated cellosilk was placed over or around the flap, and the lines traced on it with brilliant green. The tracings were then transferred to sheets of paper and labeled.

OBSERVATIONS

We have grouped the data secured into three divisions depending on the types of flaps tested: (1) single-pedicled flaps, (2) double-pedicled flaps and (3) tubed flaps.

Single-Pedicled Flaps.—These flaps are tonguelike areas of skin and subcutaneous tissue which are raised and have a single pedicle. They either were transferred immediately or were sutured back and the transfer was delayed.

The flaps raised in the temporal region were in an area innervated by the trigeminal nerve. They were usually formed over the temporal

8. von Frey, M.: Untersuchungen über die Sinnesfunctionen der menschlichen Haut, Abhandl. d. math.- phys. Cl. d. k. sächs. Gesellsch. d. Wissensch. **23**:214, 1896.

artery in the direction it follows on the head. The innervation of the upper portion of the flap was cut across so that there was very little sensation left.

The flaps on the abdominal wall were raised with the pedicles more or less in a line with the courses of the nerves so that the innervation extended down the flaps almost to the ends, if they were short. In cases 5 and 6, the flaps were longer and more narrow in proportion, so that the innervation was destroyed. In case 8, the flap was wider than it was long and sensations were present over seven tenths of its length even though it had been raised across its innervation.

Summary: All the single-pedicled flaps were utilized either immediately or within two weeks after their formation so that regeneration of sensations was not found in any of them.

TABLE 1.—*Single-Pedicled Flaps*

	Case	Age	Sex	Date of Formation	Length of Flap, Cm.	Width of Flap, Cm.	Time, Days	Distance from Pedicle*	
								Prick	Touch
Flaps raised in the temporal region	1	49	M	2/13/30	8.2	2.2	12	3.0	2.6
	2	60	M	4/20/28	8.0	2.0	10	2.1	1.5
Flaps raised on the abdominal wall	3	46	M	1/ 4/27	6.0	3.4	13	4.1	3.6
	4	34	M	1/10/28	6.0	4.0	14	5.0	4.4
	5	29	M	1/25/28	12.0	3.2	4	4.0	3.5
	6	22	M	6/22/27	10.0	5.4	10	4.5	4.0
	7	32	M	3/23/27	8.5	3.8	13	6.0	5.3
	8	57	M	11/21/28	10.5	12.0	7	7.2	4.6
	9	44	M	2/14/33	8.0	5.0	9	3.0	2.5

* The figures indicate in centimeters the distances from the pedicle at which sensations were present on the flap.

The extent of the loss of sensations depended on the extent to which destruction of the nerves occurred. If only the smaller branches of the peripheral nerves were traumatized, the destruction of sensations was lessened. If a flap was cut broad and short the nerve branches in the major portion of the flap were not injured, and the sensations were present over a greater area than if a very narrow and long flap was formed. The temperature sensations were found between the lines of touch and pain.

Double-Pedicled Flaps.—These flaps are areas of skin and subcutaneous tissue which are raised between two parallel incisions and which have a pedicle at each end continuous with the skin. The flaps were either sutured back into their original beds to be used later, and at the proper time after one pedicle had been divided were shifted and sutured into their new position, or they were transferred immediately, being used as a "gauntlet." In order to simplify the neurologic survey the data on double-pedicled flaps are grouped into three tables depending on the anatomic region in which the flaps were raised.

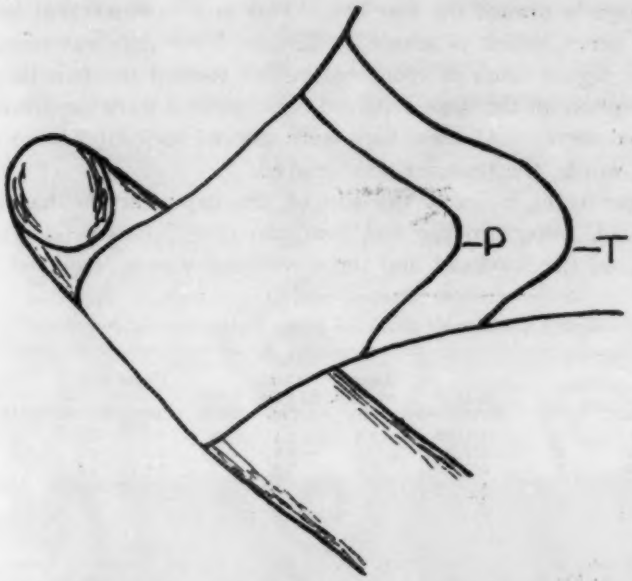

Fig. 1 (case 3, table 1).—A single-pedicled flap raised on the abdominal wall and immediately transferred to the finger. The curved line *P* indicates the limit of prick on the flap. The curved line *T* indicates the limit of epicritic touch. The tests were performed on the thirteenth day. The drawing shows the actual size of the flap and of the finger.

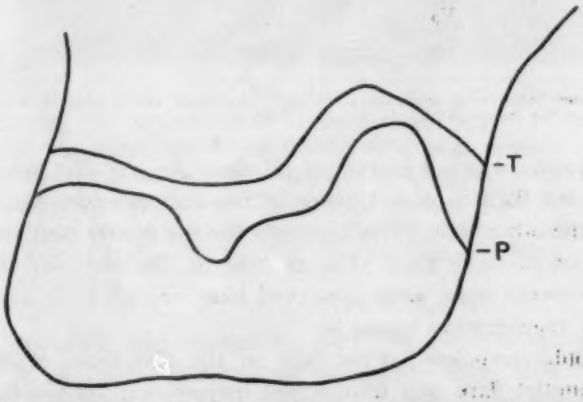

Fig. 2 (case 8, table 1).—The outside line shows the delayed transfer flap with a single pedicle formed on the abdominal wall. The curved line *P* shows the limit of prick sensation. The curved line *T* shows the limit of light touch. The tests were made seven days after the flap was raised and replaced in its own bed but before it was transferred to the hand for which it was planned. Note the types of curves developed in the tests. The illustration is one-half the actual size of the flap.

The flaps raised on the forehead were made from the root of the nose obliquely toward the hair-line. This area is innervated by the trigeminal nerve, which is sensory. In case 1 the flap was raised in the temporal region from in front of the ear toward the hair-line. With that exception all the flaps reported on in table 2 were supplied by both trigeminal nerves. All these flaps were sutured back after being formed; in other words, the transfer was delayed.

"Upper end" indicates the end of the flap near the hair-line and "lower end" refers to the end near the nose. In case 1, the upper end was on the forehead and the lower end was in front of the ear.

TABLE 2.—*Double-Pedicled Flaps Raised on the Forehead*

Case	Age	Sex	Date of Formation	Length of Flap, Cm.	Width of Flap, Cm.	Time, Days	Upper End*		Lower End*	
							Prick	Touch	Prick	Touch
1	25	M	12/15/30	9.5	2.5	13	0.5	0.0	1.5	1.0
2	34	M	3/21/28	7.5	2.5	8	1.0	0.5	1.4	1.1
3	48	F	5/16/28	7.2	2.4	7	0.8	0.2	1.5	1.0
4	55	M	11/28/32	7.7	2.4	10	1.0	0.5	0.5	0.0
5	30	F	12/31/27	6.7	2.6	10	0.8	0.4	1.2	0.7
6	30	M	4/ 6/31	7.3	2.4	12	0.6	0.2	1.1	0.4

* The figures indicate in centimeters the distances from the pedicle at which sensations were present on the flap.

TABLE 3.—*Double-Pedicled Flaps Raised on the Abdominal Wall.*

Case	Age	Sex	Date of Formation	Length of Flap, Cm.	Width of Flap, Cm.	Time, Days	Upper End*		Lower End*	
							Prick	Touch	Prick	Touch
1	26	M	3/31/30	11.0	5.5	10	5.5	5.0	2.0	1.5
2	29	F	4/13/27	17.0	8.0	10	4.2	3.5	4.0	3.2
3	34	M	1/ 9/28	13.5	6.2	8	4.0	3.5	5.0	4.5
						26	No change			
4	55	M	7/14/30	11.0	6.0	15	3.5	3.0	2.6	2.0

* The figures indicate in centimeters the distances from the pedicle at which sensations were present on the flap.

The innervation was cut in raising all these flaps. The lower ends of all, except the flaps in case 1, were in areas supplied by the trigeminal nerves of the other side. This accounts for the nearly complete absence of sensations in these flaps. On account of the necessity of transfer within two weeks none were preserved long enough to determine what the rate of regeneration would be.

The double-pedicled flaps raised on the abdominal wall were all used as gauntlet flaps and transferred immediately on the hand. The innervation of this area is from the anterior terminal branches and the lateral branches of the ninth, tenth, eleventh and twelfth thoracic nerves. All these are mixed sensory and motor nerves.

These flaps were raised with the upper ends near the midline of the abdominal wall toward the costal margins and the lower ends toward

the flank almost at right angles to the courses of the nerves. The width, however, prevented the complete loss of sensations. There was no regeneration after twenty-six days.

These areas are innervated by the eleventh and twelfth thoracic nerves, the lateral cutaneous nerve of the thigh, the genitofemoral nerve,

TABLE 4.—*Double-Pedicled Flaps Raised from the Thigh, Calf and Leg*

Case	Age	Sex	Date of Formation	Length of Flap, Cm.	Width of Flap, Cm.	Time, Days	Upper End*		Lower End*	
							Prick	Touch	Prick	Touch
Thigh										
1	28	M	1/ 5/27	23.0	12.0	10	11.0	6.5	1.0	0.0
2	50	M	12/ 5/22	7.0	5.0	10	2.6	2.0	1.9	1.3
Calf of leg										
3	21	M	11/ 8/29	12.6	5.5	10	3.7	3.2	1.4	1.0
4	24	M	1/ 8/29	10.5	5.2	12	3.5	2.7	1.8	1.2
5	21	M	12/30/29	13.0	6.0	11	4.1	3.5	1.5	1.1

* The figures indicate in centimeters the distances from the pedicle at which sensations were present on the flap.

Fig. 3 (case 1, table 4).—Delayed transfer flap with a double pedicle raised from the thigh. A shaped piece of rubber dam had been placed between the flap and thigh. The curves marked on the flap indicate the limits of the sensations. The lines *1* and *1'* show the limit of prick sensation. The lines *2* and *2'* show the limit of temperature sensation. The lines *3* and *3'* show the limit of light touch sensation. Note that at the lower end of the flap toward the knee the sensations are absent beyond the limit of the flap. The readings were taken on the tenth day after raising the flap.

the intermediate and medial rami of the femoral nerve, the lateral cutaneous nerve of the leg, the saphenous nerve and the superficial peroneal nerve. The lateral cutaneous nerve of the thigh is a sensory nerve, and all the others are mixed sensory and motor nerves.

"Upper end" refers to the end of the flap highest up on the extremity. All these flaps were formed in a direction parallel to the course of the nerves. The upper ends therefore have much more innervation than the lower.

Summary: All the double-pedicled flaps with the exception of those raised on the thigh and leg were formed across the courses of the nerves. The flaps on the forehead were narrow and had very little sensation. Those on the abdominal wall were half as broad as long and had sensations in both pedicles even though they had been raised across the courses of the nerves. The upper ends of the flaps raised on the thigh had more sensation than the lower ends because they were formed in a direction parallel to the course of the nerves.

Tubed Flaps.—Tubed flaps are double-pedicled flaps in which the edges are sutured margin to margin, thus making a tube completely covered by skin and enclosing the subcutaneous tissue. The transfer on all tubed flaps is necessarily delayed. The data on the tubed flaps are grouped into four tables depending on the anatomic areas in which the flaps were raised.

TABLE 5.—*Tubed Flaps on the Neck*

Case	Age	Sex	Date of Formation	Length of Tube, Cm.	Circumference, Cm.	Time	Upper End*		Lower End*	
							Prick	Touch	Prick	Touch
1	8	M	3/14/27	11.5	4.5	13 days	2.5	2.2	2.4	2.0
2	48	M	12/16/29	11.0	4.3	12 days	2.4	1.5	2.0	1.6
3	6	F	1/18/29	10.7	4.0	10 days	2.3	1.8	2.0	1.3
4	16	F	4/ 2/28	10.3	4.6	4 days	2.0	1.0	1.0	0.5
					4.4	1 mo.	2.7	2.2	1.8	1.0
					4.3	7 mos.	Sensations all present			

* The figures indicate in centimeters the distances from the pedicle at which sensations were present on the flap.

The flaps were often formed with the upper pedicle behind the ear at about the level of the hair-line and ran from this point diagonally across the neck with the lower pedicle above or below the clavicle. These flaps were usually raised in the area innervated by the anterior branches of the second, third and fourth cervical nerves, which help to form the cervical plexus and emerge as the following cutaneous nerves: the lesser occipital, the great auricular, the cutaneous nerve of the neck and the supraclavicular nerves. These are all pure sensory nerves.

"Upper end" refers to the end of the tube on the head and "lower end," to the end on the neck or chest. The sensation of temperature was felt between the lines of prick and touch.

These tubes were raised across the courses of the cutaneous nerves destroying the innervation along the shafts and leaving only a short portion with sensations at each end. More than half of the length of every tube was without sensations.

Inasmuch as these four tubes are all approximately the same length and circumference, we can consider the regeneration as one complete picture. Apparently there was no regeneration of sensations in from

four to ten days. The slight edema present after the formation of the tube could account for the difference in the readings at four and at ten days by causing a dulness which would obscure the definite limit of sensation. In one month there was a definite advance in the returning sensations, and they had completely returned in seven months. The sensations must have been carried in by the great auricular nerve above and the middle and anterior supraclavicular nerves below, since the pedicles were in the regions innervated by these nerves.

The flaps raised on the arm were made on the inner side with the upper pedicle near the axilla and the lower toward the elbow. This area is innervated by the axillary nerve, the posterior cutaneous nerve of the arm, the medial cutaneous nerve of the arm and forearm and

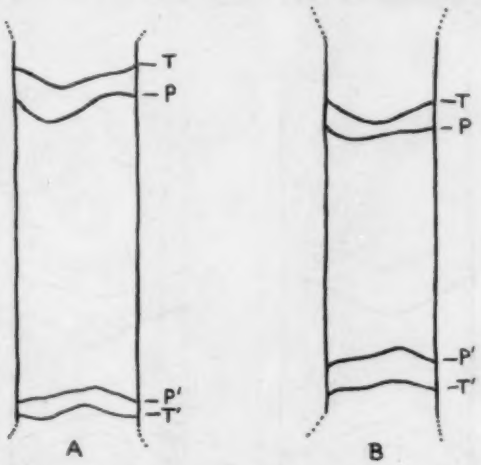

Fig. 4 (case 4, table 5).—Tracings of sensation tests on a tubed flap raised from the neck (one-half actual size). *P* and *T* indicate the lines of prick and light touch sensation on the upper end of the tube. *P'* and *T'* indicate the lines of prick and touch on the lower end of the tube. *A* shows the tracing made four days after the tube was formed; *B*, the tracing on the same tube made one month after the tube was raised. Note that the sensations do not advance in even, regular lines. The readings taken for the tables are the points of greatest advance measured from the base of the tube. The sensations advance from both ends, finally meeting somewhere on the shaft. There has been an appreciable gain in sensations during one month as can be noted by comparing *A* and *B*. The tracings were made on transparent material which was wrapped around the tubed flap and then spread out and redrawn.

the intercostobrachial nerve. The axillary and the posterior cutaneous nerves are mixed nerves while the others are pure sensory nerves.

"Upper end" refers to the end of the tube toward the axilla and "lower end," to the end of the tube toward the elbow. The sensation of temperature was felt between the lines of touch and prick.

These tubes were raised in a direction about parallel to the course of the nerves so that the innervation of the skin used in the tubes was not as greatly interfered with as in the first series of tubed flaps

TABLE 6.—*Tubed Flaps Raised on the Arm*

Case	Age	Sex	Date of Formation	Length of Tube, Cm.	Circumference, Cm.	Time	Upper End*		Lower End*	
							Prick	Touch	Prick	Touch
1	25	M	1/22/30	10.0	4.0	10 days	5.1	4.5	2.7	2.3
2	35	F	10/ 9/29	10.2	4.3	7 days	5.0	4.4	2.5	2.0
3	32	F	6/21/29	10.4	4.0	6 days	5.4	4.7	2.6	2.2
4	31	F	2/10/32	10.0	4.3	10 days	4.8	4.2	3.0	2.4
5	21	M	2/13/33	12.2	5.1	2 days	6.1	5.0	3.1	2.5
					5.0	11 days	6.3	5.2	3.2	2.7
					4.8	1 mo.	6.8	5.5	3.5	3.0

* The figures indicate in centimeters the distances from the pedicle at which sensations were present on the flap.

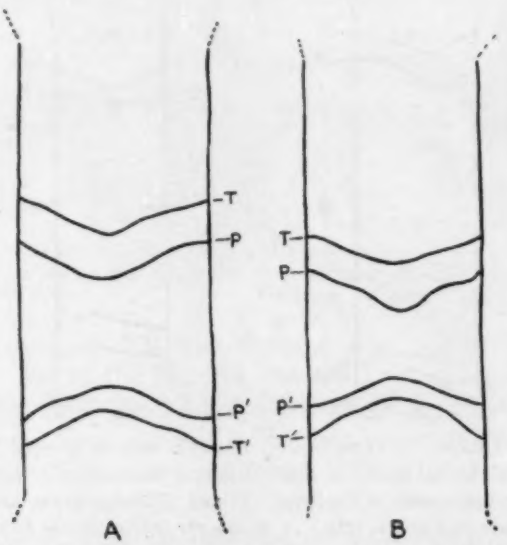

Fig. 5 (case 5, table 6).—Tracings of tests on a tubed flap raised from the arm (one-half actual size). *P* and *T* are the limits of prick and light touch on the upper end of the tube, and *P'* and *T'* are the limits of these sensations on the lower end of the tube. *A* shows the curves after two days; *B*, the curves after one month. There has been a fairly marked gain in sensations on the upper end of the flap after one month, while on the lower end the gain has been much less marked. The sensations of heat and cold are found between the curves of prick and light touch. Note that the sensations in this flap are farther down the shaft of the tube than in figure 4 because the flap was cut in the direction of the course of the innervating nerves, while the flap in figure 4 was cut across the nerves.

(table 5). The innervation of this series is therefore more completely present on the tubed flaps, as can be seen from the table. The difference in the readings in case 5 for two days and eleven days can be

accounted for by the disappearance of the edema which may have partly numbed the tube.[9] There was apparently some regeneration of sensations after one month.

TABLE 7.—*Tubed Flaps Raised on the Abdominal Wall*

Case	Age	Sex	Date of Formation	Length of Tube, Cm.	Circumference, Cm.	Time	Upper End*		Lower End*	
							Prick	Touch	Prick	Touch
1	12	F	3/25/27	14.0	4.5	10 days	4.2	3.7	2.7	2.3
2	12	M	6/18/28	13.0	5.0	9 days	3.8	3.2	3.0	2.5
3	26	M	5/11/28	14.2	5.0	10 days	3.0	2.5	2.6	2.1
4	16	M	1/12/28	12.5	5.1	12 days	3.2	2.5	2.0	1.5
5	17	M	3/13/31	10.5	5.5	10 days	2.8	2.4	1.8	1.2
					5.2	3 mos.	3.7	3.3	3.0	2.4
6	42	M	4/ 6/32	12.0	6.0	6 days	3.5	2.3	1.5	1.0
					5.5	7 mos.	5.3	4.7	3.0	2.7

* The figures indicate in centimeters the distances from the pedicle at which sensations were present on the flap.

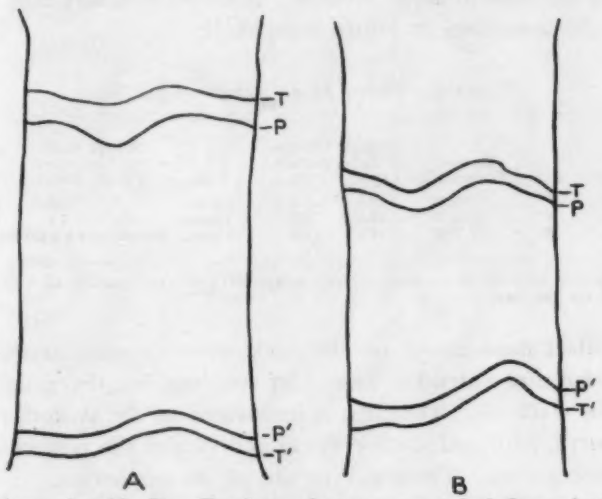

Fig. 6 (case 6, table 7).—Tracings of tests on a tubed flap raised from the abdominal wall (one-half actual size). *P* and *T* indicate the limits of the sensations of prick and light touch at the upper end of the tube near the costal margin and *P′* and *T′* indicate the limits of these sensations at the lower end of the tube on the abdominal wall. *A* is a tracing made six days after the formation of the tube. *B* is a tracing made seven months after the formation of the tube. Note the uneven line of advance of the sensations. The sensations were coming in faster from the upper end which is parallel to the normal course of the nerves in this area.

The tubed flaps raised on the abdominal wall extend from the margin of the ribs in the midaxillary line diagonally across the abdomen on the same side toward the pubis for varying distances but never

9. Postoperative transient paralyses and those caused by the use of crutches may possibly be explained on the same basis.

beyond the midline. This area is innervated by the anterior terminal branches and the lateral branches of the ninth, tenth, eleventh and twelfth thoracic nerves. All of these nerves are mixed nerves.

"Upper end" refers to the end of the tube near the costal margin and "lower end," to the end toward the pubis. The temperature sensations were felt between the lines of light touch and prick.

These tubes were raised across the courses of the nerves so that the innervation to the greater part of the tubes was destroyed. About one half of the tube did not have sensation. The sensations regenerate from both ends gradually toward the center of the shaft of the tube. The upper end retains its sensations for a longer distance than the lower end because this end is more in line with the course of the nerves. In case 5 the sensations came back in about two thirds of the tube in three months, and in case 6 they regenerated in about three fourths of the tube in seven months. It would probably take about one year for the sensations to return completely.

TABLE 8.—*Tubed Flaps Raised on the Back*

Case	Age	Sex	Date of Formation	Length of Tube, Cm.	Circumference, Cm.	Time	Upper End*		Lower End*	
							Prick	Touch	Prick	Touch
1	28	F	5/10/27	42.0	5.2	3 wks.	3.5	3.0	4.3	3.5
2	43	F	5/ 3/27	35.5	6.0	3 mos.	6.5	4.5	7.0	6.0
3	48	M	3/ 2/26	18.0	5.0	17 mos.	Sensations all present			

* The figures indicate in centimeters the distances from the pedicle at which sensations were present on the flap.

The tubed flaps raised on the back were elevated at the level of the shoulder and extended down for varying lengths usually to the level of the sixth rib. This area is innervated by the posterior branches of the fourth, fifth and sixth cervical nerves and the posterior rami of the thoracic nerves. These nerves are all mixed nerves.

"Upper end" refers to the end of the tube near the shoulder and "lower end" to the end down the back. The temperature sensations were found to be present between the lines of prick and touch sensation. In cases 1 and 2 the tubes were of considerable length and were formed with islands of tissue about half way down by de River's method, thus forming really two tubes. Sensations were absent in these islands of skin.

These tubes were formed across the courses of the nerves so that most of the innervation was destroyed. Sensations were therefore present only a short distance on the tubes. In case 3 the tube was shorter and the sensations were all present in seventeen months.

Summary: All the tubed flaps are of about the same length and diameter, with the exception of those raised on the back. Healing was by first intention without infection.

Two factors influence the regeneration of sensations: the relation of the direction of the tubed flaps to the course of innervating nerves, and the type of innervation. All the tubes with the exception of those raised on the arm and the upper ends of those raised on the abdominal wall were formed across the courses of the innervating nerves. The tubed flaps with the exception of those raised on the neck were in areas innervated by mixed nerves. The area on the neck where the flaps

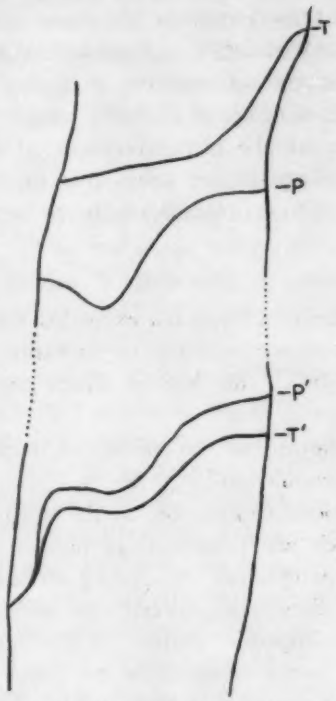

Fig. 7 (case 2, table 8).—Tracings of tests on a tubed flap raised from the back, after three months (one-half actual size). *P* and *T* indicate the limits of prick and light touch on the upper end of the tube raised on the back. *P'* and *T'* indicate the limits of these sensations on the lower end of the tube. The broken line represents the length of the shaft which is not shown in the drawing. This tube was 35.5 cm. in length.

were raised is innervated by pure sensory nerves. The tubes on the arm were not formed in the areas of the sensory nerves.

When the tubed flaps were formed across the paths of the nerves most of the innervation was destroyed regardless of the type of innervation. The tubes on the arm (table 6), which were raised in the direction of the nerves, had sensations for much longer distances than any of the others. The upper ends of the tubes raised on the abdominal

wall (table 7) had sensations for longer distances in proportion to the sensations of their lower ends than any of the other sets of tubed flaps.

The regeneration of sensations was much more rapid in the tubes raised in the areas of pure sensory nerves than in the areas innervated by mixed nerves. In case 4, table 5, a tube 10.3 cm. long had recovered its sensations in seven months, whereas a tube 12 cm. long on the abdominal wall (case 6, table 7) had recovered sensations for about three fourths of its length in the same time. A tube 18 cm. long on the back (case 3, table 8) had recovered sensation in seventeen months, a much slower rate of recovery than that for the tube on the neck (case 4, table 5), which was 10.3 cm. long.

The measurements of the circumferences of the flaps show that there is a slight shrinkage in the tubes due to the contracting scar; this is not great enough to contraindicate the preservation of tubes over long periods of time.

COMMENT

The loss of epicritic touch always exceeded the loss of pain in all the pedunculated flaps tested, and the regeneration of the sensation of pain was always first in all the flaps in which regeneration had taken place.

A review of the anatomy of the superficial nerves will facilitate the explanation of this phenomenon.[7]

The general sensations represented at the periphery are carried by cutaneous nerves which are processes of bipolar cells located in the posterior root spinal ganglions. According to the most widely used theory there are two distinct superficial systems: the protopathic and the epicritic. The protopathic system is the more primitive, and through it the grosser forms of sensation are conveyed. It gives information of pain and of extreme degrees of heat and cold and is not sharply localized. The epicritic system carries information of finer tactile impressions and mild degrees of heat and cold and is finely graded and definitely localized.

All these fibers enter the spinal cord through the posterior nerve roots, and a regrouping immediately takes place. All sensations of a similar nature, whether protopathic, epicritic or deep, are grouped together, with the exception of a few tactile fibers. There are only four groups in the spinal cord: thermal, pain, tactile and muscle sensations. The fibers carrying thermal, pain and tactile sensations end around cells at the tip of the posterior horn of the cord, and a new set of fibers from these cross to the opposite side of the cord to form the spinothalamic tracts. A few of the fibers of epicritic touch remain

on the same side of the cord with the fibers carrying muscle sensations continuing up in the columns of Goll and Burdach which end in the medulla oblongata, in the gracile and cuneate nuclei. New fibers from these form the mesial fillet which is joined farther on by the spinothalamic tracts. In the pons and midbrain the mesial fillet is divided into two parts: mesial and lateral. The mesial part contains the fibers conveying muscle sensations, and the lateral part carries the thermal, pain and tactile sensations. The mesial fillet ends in the thalamus, and new fibers carry the sensory impulses partly to the essential organ in the thalamus but mainly to the cerebral cortex. The thalamus has the power to recognize certain sensations in a crude manner but is unable to localize them. The finer analysis of sensations is made in the cerebral cortex.

If the spinal cord is injured general sensations will be lost to all parts the nerves of which enter the cord below the point of injury. The demarcation will be the same for all sensations whether they are epicritic or protopathic because the sensations have already been regrouped according to kind. If a nerve is injured before it reaches the cord, the loss of sensations will be in proportion to the extent to which they are carried by the nerves involved. The unit of protopathic supply lies in the posterior roots. No one nerve forms more than a tributary supply of an area innervated by a plexus of nerves, and whenever a single peripheral nerve is destroyed the loss is not complete. Other branches of the same plexus carry pain fibers to the same area by a slightly different route, and these may not have been injured by the trauma. If the injury is extensive enough the area may lose all of its sensations, but the loss will not be as extensive as it would be if only one nerve carried all the sensations to that area. This also explains the more rapid regeneration of the protopathic sensations. Since the sensation of touch as elicited by light pressure is a protopathic sensation, many observers have been led to believe that light touch returns before or with pain instead of after it.

The peripheral nerves form the units of epicritic supply. Each peripheral nerve carries the epicritic sensations from its own area, and the other nerves of the same plexus do not report from the same general area but from specific parts of that area. The loss of epicritic touch sensation is therefore more marked than that of prick or pain. Protopathic temperature sensations are reported in the same manner as pain. However, there are fewer nerve endings for temperature sensations in the skin so that the limits are hard to locate, especially since the manner of testing involved some slight pressure when the skin was touched with the test tubes.

Cutting of the nerves causes a wallerian degeneration [10] of the peripheral stump and some degeneration of the proximal ends. The peripheral stump degenerates rapidly, but all of its constituent parts do not disappear. The parts such as the axon and the myelin which trophically depend on the nerve cell are destroyed, but the parts which do not depend on the influence of the neuron undergo changes which leave them ready to receive and guide the new axons when they begin to grow out. There are tubes empty of axons waiting for the regenerating axons to return to the end-organs. The new axons come in all directions in great disorder seeking the empty tubes and trying to connect with the end-organs. The end-organs apparently have some attraction for the axons so that the axons of epicritic touch seek the end-organs of the same sensation and so on.

In the pedunculated tubed flaps formed across the nerve courses the empty nerve tubes were at right angles to the course of the regenerating nerves. The regenerating nerve axons therefore had to come to the ends of the empty tubes and then go across to the nerve endings or make new channels directly to the end-organs. Either course would cause the regeneration to be much slower than if the direction of the empty tubes and that of the regenerating axons were the same. This was demonstrated in our cases. The tubed flaps raised on the neck and abdominal wall were formed across the course of the nerves while the tubed flaps raised on the arm were parallel to the course of the nerves. The regeneration of the sensations was much faster in the flaps on the arm than in either of the other two groups.

Another factor enters into the rate of regeneration. Some of the peripheral nerves conveying general sensations come from nerves which are purely sensory while others come from nerves which also give motor fibers to muscles before ending in the sensory peripheral branches. These so-called motor nerves are apparently composed of both sensory and motor nerve fibers which separate at the cord. The rate of regeneration in these mixed nerves is slower than the rate in those which are parts of purely sensory nerves. The axons must experience greater difficulties in regenerating from the complex nerve stumps. We found that the rate of regeneration was much slower in the flaps raised in the areas innervated by the mixed nerves.

It is apparent from these tests that there is no evidence of regeneration of the sensations until after the third week. A double-pedicle flap raised on the abdominal wall (case 3, table 3) showed no change in reactions to the tests twenty-six days after its formation. Tubed flaps showed an increase in sensations one month after formation. None of

10. Ramón y Cajal, S.: Degeneration and Regeneration of the Nervous System, translated by R. M. May, New York, Oxford University Press, 1928, vol. 1.

the patients could be followed after their discharge from the hospital, so that the rate of regeneration cannot be calculated. In analyzing the flaps in which sensations have partly or completely returned, we can roughly estimate the rate of regeneration at about 1 cm. per month.[11] This naturally varies with the location, width and length of the flaps because all these factors aid or retard the growth of the axons. A tubed flap 10.3 cm. long and 4.6 cm. in circumference raised on the neck (case 4, table 5) showed a return of sensations of 1 cm. per month. A tubed flap 10.5 cm. long and 5.5 cm. in circumference raised on the abdominal wall (case 5, table 7) showed a return of sensations of 0.7 cm. per month, and a second tube (case 6, table 7) 12 cm. long and 6 cm. in circumference also raised on the abdominal wall showed a rate of regeneration of 0.5 cm. per month. Neither of these tubes had completely received their sensations at the time of the test, and it is problematic whether the rate would have changed later on if the tubed flaps had been kept intact. A tubed flap raised on the back (case 3, table 8) had recovered all sensation after seventeen months. We do not know, however, when this return had been completed.

The clinical value of these observations is important. Inasmuch as the nerve supply in pedunculated flaps has been interfered with more or less seriously the patient is not warned by pain as to injury. Therefore great care must be exercised when handling flaps and applying dressings to avoid injury, because the normal sensations which would convey this information of danger are absent. Compresses which are too hot or dressings which are so tight as to interfere with circulation will not be noted by the patient. Tissues in which protopathic sensations are lost apparently do not heal as readily as normal tissue. We have noted that tubed flaps transplanted after the sensations have completely returned appear to heal better than those transplanted before this regeneration has returned, but the fact that the blood supply in these flaps is also completely adequate must also be borne in mind.[12]

Apparently age has no influence on the amount of degeneration or on the rate of regeneration of superficial sensations. In our series, composed of patients ranging from 6 to 60 years, no definite difference was found.

SUMMARY

There are two superficial systems of peripheral sensations depending on two sets of nerves. The extent of loss of sensations depends on

11. The rate of regeneration as observed by us is considerably slower than that noted in the textbooks in which the rate is usually given as about 1 mm. per day when nerves have been divided and sutured.

12. German, W.; Finesilver, E. M., and Davis, J. S.: The Establishment of Circulation in Tubed Skin Flaps. An Experimental Study, Arch. Surg. **26**:27 (Jan.) 1933.

the extent to which nerve destruction occurs. The degree of the loss depends to a certain extent on the direction of the pedunculated flap in regard to the direction of the innervating nerves. In pedunculated flaps the loss of pain is always greater than the loss of epicritic touch.

Temperature sensations were usually found between the lines of prick and touch. The nerve supply in newly formed pedunculated flaps is usually interfered with to such a degree that every care must be taken to protect the flap from injury. The regeneration of sensation appears to be faster in flaps raised in areas innervated by pure sensory nerves than in areas innervated by mixed nerves.

GASTRIC ACIDITY AS INFLUENCED BY PYLORIC CLOSURE AND STENOSIS

ROBERT ELMAN, M.D.
AND
C. T. ECKERT, M.D.
ST. LOUIS

It has become increasingly evident that the acidity of gastric contents depends not entirely on variations in the secretory activity of the stomach, but also on the degree to which the secreted acid is neutralized. It has been demonstrated, for example, that pure gastric juice, actively secreted, reaches a constant acidity of about 0.5 per cent hydrochloric acid (about 140 degrees). As found in normal gastric contents after an adequate stimulus, the acidity is much lower, indicating that this value has been reduced until it is usually about from one third to one fourth of this level. Although it is generally agreed that neutralization brings about this reduction, there is still some dispute about its mechanism.

From a variety of evidence summarized in previous communications from this clinic,[1] it appeared that this neutralizing action took place in the stomach largely by the action of regurgitated alkaline pancreatic juice, which combined with the hydrochloric acid and thus kept gastric acidity within limits usually designated as normal. If this theory holds true, it is obvious that whatever initiates regurgitation, the pyloric sphincter must play a decisive rôle by controlling the degree to which reflux can occur. We accordingly investigated the relation between the activity of the sphincter and the neutralization of gastric acidity. In our first experiments,[1c] we produced an insufficiency of the sphincter by performing a careful pyloromyotomy, after which we noted a marked and persistent lowering of gastric acidity, shown by a more rapid and complete neutralization of an acid test solution. The present paper is concerned with a series of observations already mentioned in a brief preliminary note,[2] in which the converse experiment was performed;

From the department of surgery, Washington University School of Medicine, and Barnes Hospital.

1. (*a*) Elman, R.: Probable Influence of Pancreatic Juice in Regulation of Gastric Acidity, Arch. Surg. **16**:1256 (June) 1928; (*b*) Surg., Gynec. & Obst. **49**:34, 1929. (*c*) Elman, R., and Rowlette, A. P.: Rôle of Pyloric Sphincter in Behavior of Gastric Acidity, Arch. Surg. **22**:426 (March) 1931.

2. Elman, R., and Eckert, C. T.: Proc. Soc. Exper. Biol. & Med. **30**:1343, 1933.

i. e., partial or complete pyloric closure was produced, and its influence on the behavior of gastric acidity was then studied.

PREVIOUS OBSERVATIONS

A number of investigators produced partial pyloric stenosis experimentally. Bolton,[3] in 1909, did so by encircling the pylorus of twenty-nine cats with a rubber tube of appropriate size. Although he did not especially study the acidity of the contents of the stomach, he observed that experimental gastric ulcers in the cats which survived showed definite evidence of delayed healing, sclerosis and incomplete regeneration, as compared with the rapid healing in cats without pyloric stenosis. Tumpeer and Bernstein [4] injected liquid petrolatum under the pyloric muscle of six dogs, but were unable to produce a stenosis. Although the dogs were observed for seven months, there was no change in the gastric emptying time, and no dilatation of the stomach was found at autopsy. No measurements of acidity were reported.

Of more direct application to the present study are the experiments of Hamburger and Friedman,[5] who tied a silk ligature about the pylorus of dogs and studied the acidity of the gastric contents before and after operation. In ten dogs, a complete stenosis was produced; as might have been expected, a fatal outcome developed within a few days, undoubtedly from dehydration and alkalosis due to vomiting. In ten other dogs, a silk ligature was tied loosely. The result was a moderate stenosis which brought about slight or no changes in acidity, but which may be considered as a control observation for the third series of nine dogs in which a marked stenosis was effected. These animals had symptoms, lost weight and died in from three weeks to two months. The acid values after a test meal were much higher than before operation, and the contents of the fasting stomach showed acidities as high as 90 degrees, whereas acid was rarely found in normal controls. Of considerable interest, too, is the fact that two of these animals were described as dying of general peritonitis from perforation of a spontaneous duodenal ulcer located just beyond the site of the occluded pylorus.

Ivy, Droegemueller and Meyer [6] studied gastric acidity as influenced by pyloric stenosis, which was produced by means of a tape or a metallic band. The dogs were also provided with Pavlov pouches, and the acidity of the pure gastric juice obtained from them was studied. The

3. Bolton, C.: Proc. Roy. Soc., London, s.B **82**:233, 1909.

4. Tumpeer, I. H., and Bernstein, M. A.: Experimental Pyloric Stenosis, Am. J. Dis. Child. **24**:306 (Oct.) 1922.

5. Hamburger, W. W., and Friedman, J. C.: Contributions to the Experimental Pathology of the Stomach, Arch. Int. Med. **14**:722 (Nov.) 1914.

6. Ivy, A. C.; Droegemueller, E. H., and Meyer, J. L.: Effect of Experimental Pyloric Stenosis on Gastric Secretion, Arch. Int. Med. **40**:434 (Oct.) 1927.

results, in general, were somewhat equivocal. However, in two of the seven dogs, the acidity of the contents of the main stomach was measured. In these animals the acid value after a test meal reached a high point of 158 and 130 degrees, respectively, which is far greater than occurs normally; it is equal, in fact, to the high acidity of pure, actively secreted juice. Of additional interest is the fact that in one of the dogs a perforating duodenal ulcer was found at autopsy. Similar experiments were described by Zukschwerdt,[7] who produced pyloric stenosis by a strip of fascia in dogs previously provided with a pavlov pouch and showing a standard secretion response. The secretion of the pouch after stenosis was produced was more prolonged and 50 per cent greater in amount. The high acidity of the pure juice secreted by the pouch remained the same, from 0.4 to 0.5 hydrochloric acid, which is the maximum acidity ever developed by the gastric juice. Unfortunately, no studies of the acidity of the contents of the main stomach were made. The prolonged emptying time, shown by roentgenogram after a meal of barium sulphate, demonstrated that a marked pyloric stenosis had been produced. Adequate control experiments were also described. At autopsy, the mucosa of the main stomach showed marked hyperemia and erosions in the lesser curvature; the mucosa of the pouch was normal. Webster and Armour [8] described dogs with pyloric obstruction kept alive through jejunal feedings. They secreted through a gastric fistula a juice of high acidity (from 0.4 to 0.5 per cent hydrochloric acid). In two of the dogs, ulcers were observed at the site of the fistula. Hoelzel and Da Costa [9] noted that in some rats on a restricted protein diet pylorospasm developed, indicated by gastric retention, and at the same time there was definite evidence of increased gastric acidity. Boldyreff,[10] in more or less acute experiments, showed a failure of neutralization of an acid solution after the pylorus was served.

Turning to observations on man, one finds that while instances of pyloric stenosis are frequently described, the data on gastric acidity are equivocal. In many cases, the stenosis, due to cicatricial contraction of a duodenal ulcer, was of such long duration that gastric dilatation and stasis had undoubtedly affected the secretory power of the mucosa. Delayed or absent neutralization of an acid test solution was found in several of such cases by one of us (Dr. Elman).[1b] In other cases described as hypertrophic pyloric stenosis in adults, definite hyperacidity was described.[11]

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7. Zukschwerdt, L.: Ztschr. f. d. ges. exper. Med. **79**:578, 1931.
8. Webster, D. R., and Armour, J. C.: Canad. M. A. J. **27**:240, 1932.
9. Hoelzel, F., and Da Costa, E.: Proc. Soc. Exper. Biol. & Med. **29**:979, 1929.
10. Boldyreff, W.: Ergebn. d. Physiol. **11**:121, 1911.
11. Bastianelli, R.: Pyloric Spasm and Its Surgical Treatment, Ann Surg. **81**:45 (Jan.) 1925.

A frequent type of hypertrophic stenosis of the pylorus occurs in infants, and one may find occasional references to the high acidity of the gastric contents of these patients. The most complete study, however, was made recently by M. J. E. Senn at the St. Louis Children's Hospital. Senn examined the gastric contents of a great many infants, and among normal controls he found, as did Marriott and Davidson [12] a few years ago, an average p_H of 3.75, with an extreme range from 2 to 5.[13] In children with hypertrophic pyloric stenosis (proved by operation), the acidity was much higher; the fasting contents showed an extreme range between p_H 1.8 and p_H 3. Moreover, no reduction of this acidity was found after a test meal of diluted cow's milk which, in normal babies, exerts a definite neutralizing action, owing to its buffer content. After operation (pyloromyotomy), a decided change was observed, the p_H showing a pronounced alkaline shift, i. e., values of 4.5 and sometimes as high as 7. This change, following relief of the pyloric barrier, could hardly be due to anything but a reflux of alkaline duodenal contents. As further evidence that this is probably the explanation, Senn noted that the gastric contents, sterile before operation, after division of the hypertrophic sphincter, often contained Bacillus coli, which could obviously have originated only by reverse peristalsis carrying intestinal contents into the stomach.[14]

METHODS

As in our previous studies, the behavior of gastric acidity was studied by means of an "acid test meal." Two hundred cubic centimeters of 0.5 per cent hydrochloric acid was introduced by a small stomach tube, and 20 cc. samples were aspirated immediately and every twenty minutes thereafter until the stomach was empty or until it was obvious that gastric emptying was delayed, in which case the retained contents were removed and measured. Samples were titrated with tenth-normal sodium hydroxide, using phenolphthalein as an indicator. A fast of twenty-four hours preceded each neutralization test. In one dog, secretion curves were obtained by using histamine as a stimulant.

Healthy adult dogs of medium size (from 6 to 10 Kg.) were used. Operations were carried out under ether anesthesia with aseptic precautions. If vomiting occurred after operation, the animal was either treated parenterally with saline solutions for several days or killed immediately with chloroform. Only animals without symptoms and in good general condition were used for postoperative observations.

In a first series of experiments, attempts were made to produce pylorospasm by encircling the pylorus with rubber elastic and, later, silver coil springs. This did not succeed, for one reason or another, so in all subsequent experiments a

12. Marriott, W. M., and Davidson, L. T.: Acidity of Gastric Contents of Infants, Am. J. Dis. Child. **26**:542 (Dec.) 1923.

13. Marriott, W. M.; Hartmann, A. F., and Senn, M. J. E.: J. Pediat. **3**:181, 1933.

14. Senn, M. J. E.: Unpublished observations.

stout silk ligature was passed around the pyloric ring and tied securely; in the tie was included the tip of a hemostat, which on removal left just enough slack to avoid a complete pyloric closure. A bit of omentum was then wrapped over the ligature to prevent adhesions. We found that the effect was apt to be more prolonged if the ligature was first soaked in 25 per cent silver nitrate, which seemed to promote scarring and lessened the tendency for the ligature to become loose. This, nevertheless, did occur not infrequently after a lapse of several weeks or months. It is possible that strips of fascia would have proved more satisfactory. After operation, neutralization tests were carried out occasionally as early as the first day; ordinarily, however, in a week or two, and in a few instances in a month or more. Autopsies were performed in all cases. Some dogs died spontaneously of pneumonia or of other causes not connected with the experiment at various times after operation. The others were killed with chloroform.

In a second series of dogs, at operation we installed a pyloric snare in order to be able to open or close the pylorus at will in the unanesthetized animal. The snare described by Maddock [15] was first tried, and in a few dogs significant observations were made. A ligature is passed around the pylorus, and the ends are carried through a glass tube and brought out through the abdominal wall, one on each side of the incision, the glass tube remaining in the abdomen after the wound is closed. Now, by drawing out on the two ends, traction is exerted around the pylorus, thus closing it against the deep end of the tube. This device generally worked well for a few days but, as might be expected, infection soon set in, whereupon it was necessary to terminate the experiment. We later used a small silver tube, about 2 mm. in diameter, provided with two tiny loops or holes at one end. A gold wire was attached loosely to one of the loops; the other loop was sutured to the anterior wall of the pylorus. The free end of the wire was passed around the sphincter and led through the tube and out of its other end, which was then made to traverse the abdominal wall through a separate tiny puncture wound in the right lumbar region. Omentum was wound around the tube and the incision was closed. The free end of the silver tube holding the free end of the wire was protected by strapping a thin wicker basket over it. Observations were started within a few days and, when possible, continued for several weeks after operation. The usual test solution of 200 cc. of 0.5 per cent hydrochloric acid was given by a stomach tube, and samples were withdrawn every twenty minutes. By drawing the wire out (a stickpin clasp passed over the wire kept it from slipping back), the pylorus was constricted; by pushing it in, it was released. Its effect on the neutralization of the test solution was observed. The greatest difficulty, in any case, was knowing how much tension to exert, particularly after several weeks when a good deal of inflammatory tissue had grown around the apparatus. The eventual scarring, too, often made repeated observations impossible, for in such a case neutralization of the acid solution did not occur even when the snare was kept loose.

EXPERIMENTAL FINDINGS

Permanent Partial Pyloric Stenosis.—In this group, there were twelve dogs in which a definite delay in the neutralization of the acid test solution was found after pyloric stenosis was produced. Figure 1 represents the findings in six of them, and shows the ineffective

15. Maddock, S. J.: J. Lab. & Clin. Med. **17**:369, 1931.

neutralization of the acid solution after pyloric stenosis, as compared with the preoperative controls. The emptying time, shown by gastric residues, was often prolonged. Fasting contents, which normally have no titrable acidity, were examined in some of the dogs with pyloric stenosis. Their acid values were always high, and twice were 140 degrees, which is as strong as gastric contents ever get, representing, therefore, the high acidity of pure, actively secreted gastric juice.

In dog 340, in addition to neutralization curves (fig. 1), curves of gastric secretion were obtained, using 1 mg. of histamine as the stimulant, injected intramuscularly. Figure 2 shows the decided increase

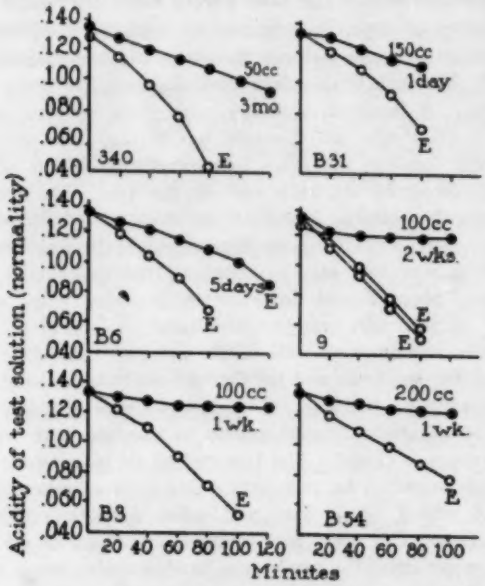

Fig. 1.—This shows the neutralization curves of six dogs before (lower curve) and after (upper curve) pyloric stenosis was produced by a silk ligature at operation. The interval in days, weeks or months is indicated in each case. *E* indicates the stomach was empty. The figures in cubic centimeters above the upper curves indicate the amount of contents removed at the conclusion of the test. The two lower curves for dog 9 were obtained before and after a loose pyloric ligature was tied; the upper curve, two weeks after a second but tighter ligature was placed.

in amount as well as in acidity of the gastric juice three months after pyloric stenosis had been produced, as compared with the preoperative control.

Control experiments, described in a previous paper,[1c] showed that simple laparotomy does not influence the rate of neutralization; in seven of the twelve dogs in the present group control curves were made before pyloric stenosis was produced. In the five in which these

were not made the postoperative change was the same as in the others. One of the twelve dogs was an inadvertent control; after a pyloric ligature was tied no change was observed, whereon a second operation was done which revealed that the tie was loose. On placing a second, tighter ligature, definite delay in neutralization was found (fig. 1, dog 9). Additional controls were also furnished by a number of the earlier experiments, when no change was noted after operation, and when autopsy showed that the ligature had slipped or had been tied loosely.

The observations at autopsy in the twelve successful experiments proved of additional interest. The stomach in some cases showed scarcely any change in size; in others, it was dilated and in some the

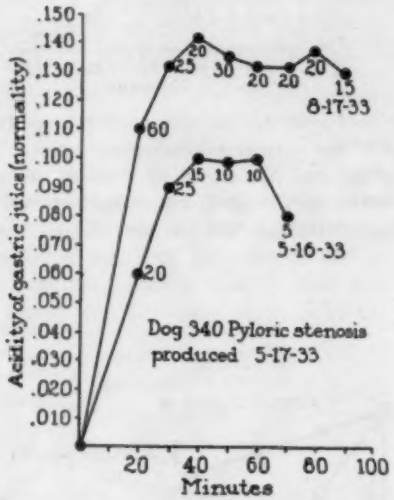

Fig. 2.—Secretion curves (after the injection of 1 mg. of histamine intramuscularly) obtained before and three months after effective pyloric stenosis had been produced. Neutralization curves for this dog are shown in figure 1. The figures refer to the amounts of gastric contents obtained. Note the greater amount (210 cc. as against 85 cc.) as well as the greater acidity with the pylorus partly occluded.

wall was hypertrophied. The site of the ligature was in all cases uninfected and covered only with scar tissue and omentum; the pylorus was free and was not adherent to adjacent structures. Pronounced constriction of the lumen of the pylorus was evident in all cases. In some, it was difficult to see how any food had been able to pass at all. With the exception of one case, in which general peritonitis from a perforated duodenal ulcer was found, the peritoneum was clear. On opening the stomach, however, a marked hyperemia of the mucosa, especially of the lesser, curvature, was evident in every case. On microscopic section, a tremendous number of oxyntic cells were seen.

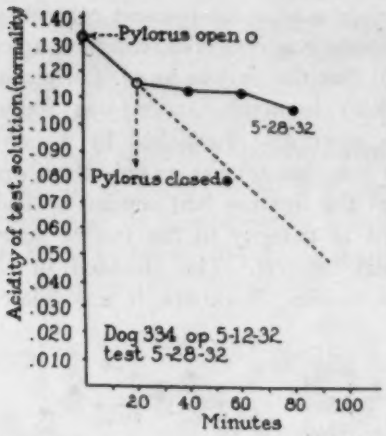

Fig. 3.—Curve obtained with the use of a pyloric snare two weeks after operation. The dotted line is the normal neutralization curve. Note the cessation of neutralization after the pylorus was closed by drawing out on the snare. In this and the following illustrations the open dots indicate titrations while the pylorus was open; the solid dots, titrations when it was closed.

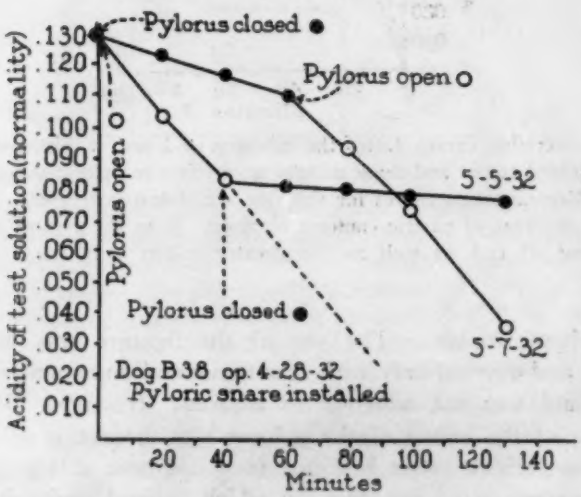

Fig. 4.—Two neutralization curves seven and nine days after operation. The upper curve shows the result when the pylorus was first closed and later opened; the lower curve, the result when it was first left open and then closed. Note the prompt drop in acidity while the pylorus was open and the delay or absence of a drop while the pylorus was closed.

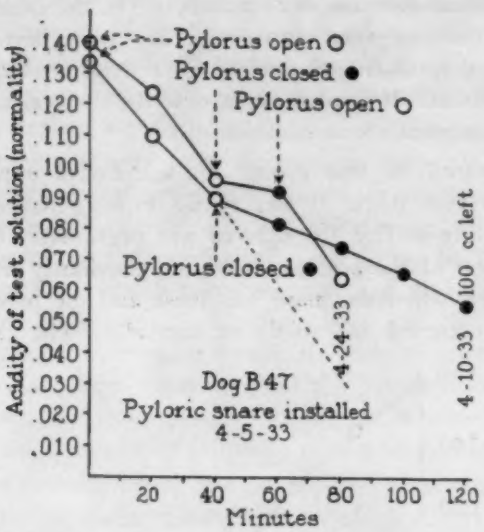

Fig. 5.—Two neutralization curves obtained five and nineteen days after operation. In the lower curve, note the delayed neutralization and emptying (as shown by the residue after eighty minutes) following closure of the pylorus. The upper curve shows three intervals: prompt neutralization with the pylorus open, none with the pylorus closed and a prompt drop of acidity when the pylorus was reopened.

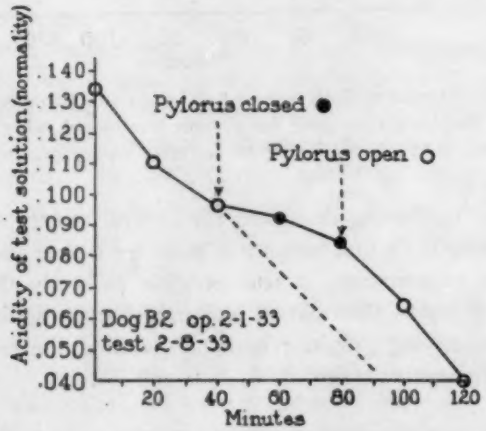

Fig. 6.—Curve for a dog with pyloric snare, seven days after operation. Note the normal drop in acid, its delay as soon as and while the pylorus was closed and its final drop as soon as it was opened again by pushing in on the snare. The broken line indicates the curve of normal neutralization.

Occasionally, small erosions were made out. In the duodenum, marked inflammatory changes were apparent. They were beyond the site of the ligature and consisted of redness, superficial erosions and an outpouring of exudate. It is planned to describe these changes in greater detail in a subsequent communication.

Pyloric Snare.—In this group, ten successful experiments were performed on seven dogs. It was found, briefly, that when the snare was drawn tightly so that the pylorus was presumably closed, little or no neutralization of the acid test solution, previously introduced, took place. However, when the snare was loose and the pylorus was open, neutralization occurred as rapidly as normally. The experiment was

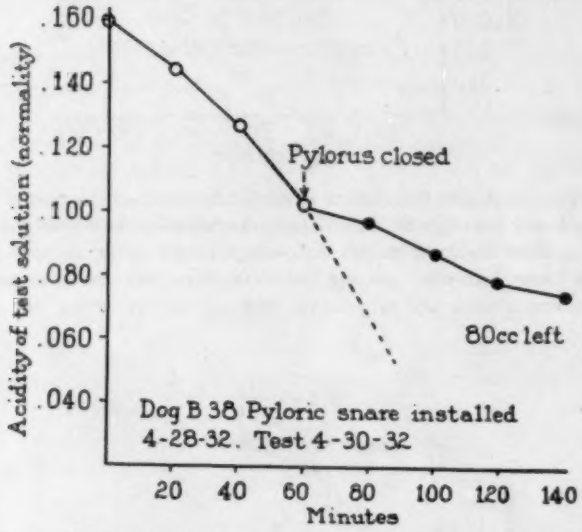

Fig. 7.—Curve obtained with the use of a pyloric snare two days after operation. Note the normal drop in acidity until the pylorus was closed, whereupon neutralization almost ceased, with a retention of 80 cc. after eighty minutes.

varied by either tightening the snare for several twenty minute periods and then loosening it, or first keeping it loose for a time and then tightening it. In two experiments, it was possible to study three intervals: with the pylorus open, then closed and finally open again (figs. 5 and 6). The accompanying graphs represent seven of the ten experiments and are self-explanatory (figs. 3, 4, 5, 6 and 7).

COMMENT

A correlation between the level of gastric acidity and the activity of the pyloric sphincter had long been suspected and was made the basis of the well known theory of Cannon, which associated the opening

and closing of the pylorus with the presence of acid in the stomach and duodenum. This theory of the "acid control of the pylorus," based on convincing experimental data, has been more or less universally accepted since it was enunciated in 1907, although Cannon himself pointed out that it failed to explain a good many facts.[16]

The present experiments were designed to study this relationship, but not by observing changes in the pylorus as influenced by gastric acidity, since it is notoriously difficult to know in an intact animal when the sphincter is open or closed. To do so by measuring the emptying time of the stomach is not accurate, for we now know [17] that other factors, such as gastric peristalsis, tone and the rapidity with which the duodenum empties, influence the rate of gastric evacuation as much as or more than the activity of the pylorus. In view of this intrinsic difficulty, it seemed more promising to induce definite change in the pylorus and measure its influence on the level of gastric acidity.

The findings described here are definite and consistent. They show not only that stenosis of the pylorus leads to a high acidity of the fasting contents, but that acid introduced into the stomach cannot be neutralized as completely or rapidly as normally. In some experiments, there was no neutralization after pyloric stenosis was produced. High acidity with pyloric stenosis was noted by other workers both experimentally and clinically, but it was attributed by some [5] to the associated gastric retention which prolonged the secretory phase because of impaired emptying. This can hardly be the explanation of the present findings, for no secretory stimulus was invoked (if we except a slight mechanical effect due to the introduction of the solution used as a test). The delay in neutralization must have been directly connected with the pyloric stenosis. Moreover, in our second series of experiments with the pyloric snare when the stenosis was transient, the same effect was observed; while the pylorus was open, gastric acidity was reduced effectively, and while it was closed, it was reduced slowly or not at all. These findings suggest that the high acidity found by others in cases of pyloric stenosis may also have been due, at least partly, to ineffective neutralization rather than to an increase in the secretory process as a result of the gastric retention.

Of greater significance is the cause of the impaired neutralization resulting from pyloric stenosis or closure. It seems difficult or impossible to explain it on the basis of an intragastric mechanism. How any diluting fluid, suddenly elaborated, or mucus suddenly secreted, could account for the prompt changes noted in our second series of experiments,

16. Cannon, W. B.: Am. J. Physiol. **20**:283, 1907.

17. Alvarez, W. C.: The Mechanics of the Digestive Tract, ed. 2, New York, Paul B. Hoeber, Inc., 1928, p. 178.

when the pylorus was opened and closed at short intervals, is hard to see. In contrast to this supposition, it is easy to understand the findings on the basis that duodenal regurgitation is the mechanism by which the neutralization is largely effected. The pyloric closure, by shutting off the duodenum, prevents reflex mainly of the alkaline pancreatic juice, which has the most efficient power of neutralizing acid in the stomach. Thus, the acid solution which is introduced remains unchanged, and by inference secreted gastric juice likewise (fig. 2, dog 340) remains higher than normal.

The assumption of duodenal regurgitation not only explains the present findings but applies equally well to the observations of Senn,[14] mentioned previously, in a comparable pyloric stenosis which occurs spontaneously in infants, and in which the high acidity of gastric contents gives way to less acid or even neutral contents promptly on release of the pyloric barrier, with many intestinal bacteria in the stomach to add further proof of regurgitation. Additional observations of a converse sort made in this laboratory lend further support to the theory of duodenal regurgitation. In these experiments, more effective neutralization of gastric acidity followed closely on successful division of the pyloric sphincter,[1c] which presumably allowed freer access of pancreatic juice into the stomach. Moreover, when pancreatic juice was drained to the outside,[1] neutralization did not occur at all. Matthews and Dragstedt[18] recently showed that neutralization fails when a valve is tied into the pylorus, making duodenal reflux impossible, even when gastric emptying is unobstructed. These observations, too, point to the importance of regurgitation in the control of gastric acidity.

It would seem from all these and other considerations mentioned in previous papers [1] that we may accept the existence of a definite correlation between the pylorus and gastric acidity, but in converse terms of that expressed by Cannon twenty-five years ago. May we not speak of the pyloric control of gastric acidity? If duodenal regurgitation is the important factor in the control of gastric acidity, it is obvious that the pylorus is a decisive link in the physiologic chain.

The anatomic changes in the duodenum, briefly mentioned here, and especially the accidental observation of a perforated ulcer in the same part of the duodenum, i. e., just beyond the exit of the stomach, have a suggestive bearing on the question of the pathogenesis of duodenal ulcer. The acid factor in peptic ulcer has received much attention in recent years,[19] and evidence is accumulating to show that

18. Matthews, W. B., and Dragstedt, L. R.: Surg., Gynec. & Obst. **55**:265, 1932.

19. Editorial, J. A. M. A. **101**:859 (Sept. 9) 1933.

it may well be the most important element. The present observations show how a high gastric acidity can be maintained, and suggest that in turn it may of itself initiate inflammatory changes which lead eventually to ulceration, hemorrhage and perforation. Experiments designed to produce this result more regularly are now in progress.

SUMMARY

Experimental pyloric stenosis leads to a spontaneous high gastric acidity, and interferes with the normal neutralization of acid introduced into the stomach. Closure of the pylorus in the unanesthetized dog delays or halts, while opening reestablishes, the normally rapid neutralization of gastric acidity. These findings add further evidence supporting the idea that duodenal reflex controls, in a large part, the level of gastric acidity. The application of these findings to a theory of the pyloric control of gastric acidity and to the pathogenesis of duodenal ulcer is commented on.

ACUTE PANCREATITIS

HARRY KOSTER, M.D.
AND
LOUIS P. KASMAN, M.D.
BROOKLYN

The increasing incidence, the relative scarcity of preoperative diagnosis, the high mortality rate and the lack of uniformity in therapy merit the many reports of acute pancreatitis which have appeared in the literature within recent years. All of the clinical bibliography is available by reference to de Takáts and Mackenzie's review.[1] They presented thirty cases of acute pancreatic necrosis in which operations had been performed by nine different surgeons during the years from 1920 to 1930. Two months later McWhorter[2] reported sixty-four cases in which operations had been performed by thirty-two surgeons, all members of the Chicago Surgical Society; in this report he presented a rather extensive review of the literature. The efforts to produce acute hemorrhagic pancreatic necrosis experimentally with a view toward elucidating the etiologic factors involved, have been thoroughly reviewed by Wangensteen, Leven and Manson.[3] It is because we believe that the accumulation of individual experiences may eventually lead to a more comprehensive appreciation of the problems associated with this disease that a report of twenty-two cases of acute pancreatitis encountered by us during the past five years is herein presented.

CLINICAL ANALYSIS

Our series well exemplifies the infrequency of the preoperative diagnosis of acute pancreatitis. Only five cases were positively diagnosed; two others were believed to be acute pancreatitis or cholecystitis, and another, perforated gastric ulcer or acute pancreatitis. Since it is necessary to observe some particular feature or group of symptoms to make the diagnosis, it is noteworthy that in 63.64 per cent of the cases these indications were absent or inconspicuous. In McWhorter's[2] series a correct diagnosis was made in eight of the sixty-four cases. In order

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From the Koster Clinic, Crown Heights Hospital.

1. de Takáts, G., and Mackenzie, W. D.: Acute Pancreatic Necrosis and Its Sequels, Ann. Surg. **96**:418 (Sept.) 1932.

2. McWhorter, G. L.: Acute Pancreatitis; Report of 64 Cases, Arch. Surg. **25**:958 (Nov.) 1932.

3. Wangensteen, O. H.; Leven, N. L., and Manson, M. H.: Acute Pancreatitis (Pancreatic Necrosis): Experimental and Clinical Study, with Special Reference to Significance of Biliary Tract Factor, Arch. Surg. **23**:47 (July) 1931.

to evaluate adequately all of the clinical aspects in our cases which were diagnosed correctly and to discover the cause for the errors in the remainder we have analyzed the symptomatology and course (table 1).

Although the age incidence varied from 17 to 78 years, 63.64 per cent of our patients were less than 35. This becomes significant when compared to the age incidence in general disturbances of the gallbladder or bile ducts, to which acute pancreatitis is linked clinically and etiologically. While cases are recorded at the age of from 2½ years up, the incidence of this condition in persons under 20 is exceedingly rare. The average age in our series was 38.27 years. McWhorter [2] found an average of 43.3 years; in half of the thirty cases reported by de Takáts and Mackenzie [1] the patients were between the ages of 40 and 60. It is also noteworthy that of our twenty-two patients, 36.36 per cent were men and 63.64 per cent women, which is in accordance with the observation of others.

Examination of the histories elicited symptoms of disease of the biliary tract in 63.64 per cent of the cases. The symptoms appeared from three weeks to ten years prior to the onset of the acute pancreatitis. In the remainder of the cases there was no relevant past history.

The illness prior to operation varied from one day to two weeks. In 40.9 per cent of the cases it occurred within twenty-four hours. In 63.64 per cent there was a sudden onset of pain in the epigastrium or right upper quadrant or both, which was soon followed by vomiting. In the remainder of the cases the onset was less precipitous but similar. Shock and cyanosis occurred in 31.8 per cent, and in these cases the diagnosis was suspected. Transient glycosuria occurred in two cases. No other significant data were observed or obtained by laboratory methods. In five cases tests for pancreatic ferments gave negative results. Hence, clinically, from the sudden onset of pain followed by vomiting, shock and cyanosis the correct diagnosis was made in four cases and was suspected in three others. In a fifth case diagnosed as acute pancreatitis accompanied by obstruction of the common bile duct by calculi and cholangeitis of two weeks' duration there was no shock or cyanosis, but the patient was deeply jaundiced. The symptomatology in the remainder of the cases suggested a variety of conditions, such as acute cholecystitis (63.64 per cent), perforated gastric ulcer (14.28 per cent) and acute obstruction of the common bile duct (22.92 per cent).

At operation the pancreas showed the typical inflammatory involvement. Fatty necrosis of the omentum and the typical serosanguineous exudate were observed in fourteen cases (63.64 per cent). Eight cases (36.36 per cent) showed fatty necrosis or the typical serosanguineous exudate. In at least 50 per cent a greenish discoloration of the fat in the gastrohepatic omentum, characteristic of this disease, was noted. In only 18.2 per cent of the cases was the pancreas the only organ in which

TABLE 1.—*Analysis of the Symptomato*

Case	Age and Sex	Gall-bladder Symptoms	Duration of Present Attack	Location of Pain	Radiation of Pain	Vomiting	Shock	Jaundice	Cyanosis	Sugar in Urine	White Blood Cell Count and Differential†	Blood Pressure: Systolic	Blood Pressure: Diastolic	Preoper… Diagno…
1	17 M	None	1 day	Epigastrium	None	+	+	0	+	0	W.B.C. 22,500 Polys. 88% Lymph. 10% Monos. 2%	112	72	Perfora… gastric…
2	33 M	None	4 days	Epigastrium	None	+	+	0	+	0	W.B.C. 10,500 Polys. 70% Lymph. 22% Monos. 2%	90	60	Acute he… orrhagic… pancrea…
3	21 M	6 mos.	1 day	Epigastrium	Right upper quadrant	+	+	0	+	0	W.B.C. 18,000 Polys. 90% Lymph. 10%	110	70	Perforat… gastric…
4	63 M	3 mos.	2 days	Right upper quadrant and epigastrium	Back	+	0	0	0	0	W.B.C. 23,000 Polys. 80% Lymph. 14%	110	90	Acute pa… creatitis… cholecys…
5	33 F	Cholecystostomy 4 yrs. ago	1 day	Right upper quadrant	Right shoulder and back	+	0	0	0	0	W.B.C. 19,600 Polys. 87% Lymph. 13%	118	72	Common… duct obs… tion due… calculus
6	32 F	Cholecystectomy 3 yrs. ago	1 day	Right upper quadrant	Right shoulder and back	+	0	0	0	0	W.B.C. 15,000 Polys. 62% Lymph. 38%	110	60	Common… duct obs… tion due… calculus
7	27 F	4 mos.	3 days	Epigastrium	Right shoulder and back	+	0	0	0	0	W.B.C. 15,900 Polys. 96% Lymph. 4% Monos. 3%	130	72	Acute ch… cystitis
8	26 F	6 yrs.	4 days	Right upper quadrant and epigastrium	Back	+	0	0	0	0	W.B.C. 12,800 Polys. 92% Lymph. 5% Monos. 3%	122	68	Common… duct cal…
9	47 M	None	3 days	Epigastrium	None	+	+	0	+	1.4%	W.B.C. 11,300 Polys. 91% Lymph. 5% Monos. 4%	90	60	Acute pa… creatitis
10	28 F	2 mos.	3 days	Right upper quadrant and epigastrium	Right shoulder and back	+	0	0	0	0	W.B.C. 18,000 Polys. 90% Lymph. 7% Monos. 3%	130	70	Acute ch… cystitis w… cholelith…
11	68 M	None	2 days	Right upper quadrant and epigastrium	Right shoulder	+	0	0	+	0	W.B.C. 33,500 Polys. 87% Lymph. 9% Monos. 4%	122	80	Acute ch… cystitis … pancrea…
12	32 F	None	3 days	Epigastrium	Back	+	0	0	0	0	W.B.C. 21,000 Polys. 82% Lymph. 18%	110	80	Acute ch… cystitis
13	27 F	3 wks.	1 day	Right upper quadrant and epigastrium	Back	+	0	+	0	0	W.B.C. 15,900 Polys. 92% Lymph. 8%	126	72	Acute ch… cystitis w… cholelith…

*Course in Twenty-Two Cases of Acute Pancreatitis**

Preoperative Diagnosis	erature; ulse; piration	Fatty Necrosis	Bloody Exudate	Gallbladder Disease	Condition of Pancreas	Operation	Complications	Results	Comment
Perforated gastric ulcer	p. 99.6 e 90 p. 20	0	+	0	Hemorrhagic necrosis	Capsule of pancreas split and drained	None	Well	Sudden onset; early fatty necrosis on pancreas only; none on omentum
Acute hemorrhagic pancreatitis	p. 103.8 e 125 p. 40	+	+	0	Hemorrhagic necrosis and edema	Capsule of pancreas split and drained; drain to lesser sac	Generalized peritonitis and paralytic ileus	Death within 5 hrs.	Sudden onset; patient was moribund at time of operation
Perforated gastric ulcer	p. 101 e 120 p. 24	+	+	Gallstones	Hemorrhagic necrosis and edema	Cholecystectomy; choledochostomy; drain to lesser sac; capsule of pancreas split and drained	None	Well	Sudden onset; marked edema of gastrohepatic omentum; pathologic report of acute cholecystitis
Acute pancreatitis and cholecystitis	p. 100 e 130 p. 20	+	+	Gallstones	Hemorrhagic necrosis and edema	Cholecystectomy; choledochostomy; drain to lesser sac; capsule of pancreas split and drained	None	Well	Slow onset with increasing pain; "coffee ground" vomitus; pathologic report of chronic cholecystitis
Common duct obstruction due to calculus	p. 99.6 e 90 p. 20	+	0	Gallbladder and common duct calculi	Hemorrhagic necrosis and edema	Cholecystectomy; choledochostomy; drain to lesser sac; capsule of pancreas split and drained	None	Well	Slow onset; pains not marked; pathologic report of chronic cholecystitis
Common duct obstruction due to calculus	p. 98.6 e 84 p. 20	0	+	Three common duct calculi	Hemorrhagic necrosis and edema	Choledochostomy; drain to lesser sac; capsule of pancreas split and drained	None	Well	Slow onset with increasing intensity of pain; head of pancreas markedly enlarged and necrotic
Acute cholecystitis	p. 100.2 e 92 p. 22	+	+	Gallstones	Hemorrhagic necrosis and edema	Cholecystectomy; choledochostomy; drain to lesser sac and gallbladder bed of liver; capsule of pancreas split and drained	None	Well	Sudden onset; head of pancreas swollen and necrotic; pathologic report of chronic cholecystitis
Common duct calculus	p. 99.6 e 92 p. 22	+	+	Gallstones	Edema	Cholecystectomy; choledochostomy; drain to lesser sac and gallbladder bed of liver; capsule of pancreas split and drained	None	Well	Slow onset; marked edema of entire pancreas; pathologic report of chronic cholecystitis
Acute pancreatitis	p. 98 e 150 p. 28	+	+	0	Edema	Capsule of pancreas split and drained	Generalized peritonitis and paralytic ileus	Death within 12 hrs.	Sudden onset; patient in moribund condition at time of opertaion
Acute cholecystitis with cholelithiasis	p. 99.6 e 84 p. 20	+	+	Gallstones	Edema	Cholecystectomy; choledochostomy; drain to lesser sac and gallbladder bed of liver; capsule of pancreas split and drained	None	Well	Sudden onset; marked edema of entire pancreas; pathologic report of acute cholecystitis
Acute cholecystitis and pancreatitis	p. 100.4 e 112 p. 30	+	+	Chronic cholecystitis; no stones	Edema	Cholecystectomy; choledochostomy; drain to lesser sac; capsule of pancreas split and drained	Pneumonia on right side	Well	Slow onset; marked edema of pancreas with a few areas of beginning necrosis; pathologic report of chronic cholecystitis
Acute cholecystitis	p. 101 e 120 p. 28	+	+	Chronic cholecystitis; no stones	Hemorrhagic necrosis and edema	Cholecystectomy; choledochostomy; drain to lesser sac; capsule of pancreas split and drained	Intra-abdominal collection	Well	Slow onset; collection broke through wound spontaneously and emptied itself; pathologic report of chronic cholecystitis
Acute cholecystitis with cholelithiasis	p. 98 e 78 p. 22	+	+	Gallstones	Edema	Cholecystectomy; choledochostomy; drain to lesser sac and gallbladder bed of liver; capsule of pancreas split and drained	None	Well	Sudden onset; marked edema of entire pancreas; pathologic report of acute cholecystitis

TABLE 1.—*Analysis of the Symptomatology and C*

Twenty-Two

Case	Age and Sex	Gall-bladder Symptoms	Duration of Present Attack	Location of Pain	Radiation of Pain	Vomiting	Shock	Jaundice	Cyanosis	Sugar in Urine	White Blood Cell Count and Differential†	Blood Pressure: Systolic	Blood Pressure: Diastolic	Preoper. Diagn.	Temperature; Pulse; Respiration	Fatty Necrosis
14	56 F	None	4 days	Right upper quadrant and epigastrium	None	+	0	+	0	0	W.B.C. 11,850 Polys. 89% Lymph. 6% Monos. 5%	128	70	Acute c cystitis cholelit	p. 101 e 132 p. 24	+
15	40 F	7 yrs.	3 days	Right upper quadrant	Right shoulder and back	+	0	+	0	0	W.B.C. 10,150 Polys. 73% Lymph. 24% Monos. 3%	138	78	Acute c cystitis common obstruc by ston	p. 100.8 e 96 p. 22	0
16	27 F	2½ yrs.	1 day	Right upper quadrant and epigastrium	Back	+	0	0	0	2+%	W.B.C. 15,200 Polys. 80% Lymph. 20%	128	68	Acute c cystitis	p. 101 e. 86 p. 22	+
17	32 F	None	1 day	Epigastrium	Back	+	+	0	+	0	W.B.C. 16,700 Polys. 90% Lymph. 7% Monos. 3%	90	60	Acute p creatiti	p. 99.8 e 84 p. 24	+
18	78 M	None	1 day	Epigastrium	Back	+	+	0	+	0	W.B.C. 14,400 Polys. 86% Lymph. 10% Monos. 4%	170	55	Perfora gastric or acute pancrea	p. 99.8 e 90 p. 28	+
19	28 M	2 mos.	1 day	Right upper quadrant	None	+	0	0	0	0	W.B.C. 13,500 Polys. 90% Lymph. 5% Monos. 5%	120	82	Acute c cystitis	p. 99.8 e 88 p. 20	+
20	31 F	6 wks.	2 days	Epigastrium	None	+	+	0	+	0	W.B.C. 14,200 Polys. 82% Lymph. 18%	112	80	Acute p creatiti	p. 101 e 92 p. 24	+
21	56 F	10 yrs.	2 days	Right upper quadrant and epigastrium	Right shoulder and back	+	0	0	0	0	W.B.C. 6,600 Polys. 70% Lymph. 22% Monos. 8%	140	80	Acute c cystitis cholelit	p. 101 e 88 p. 20	0
22	63 F	Cholecystectomy 2 mos. ago	2 wks.	Epigastrium	None	+	0	+	0	0	W.B.C. 20,000 Polys. 93% Lymph. 7%	150	80	Acute p atitis s panied common obstruc by calc choland	p. 100.6 e 116 p. 24	+

* In each case a Kocher mobilization of the duodenum was performed and the head of the pancreas was pa for calculi. The mortality was 22.7%.

† W.B.C. indicates white blood cells; Polys., polymorphonuclears; Lymph., lymphocytes, and, Monos., mononucle

Twenty-Two Cases of Acute Pancreatitis—Continued*

Preoper. Diagn.	...rature; ...ulse; ...piration	Fatty Necrosis	Bloody Exudate	Gallbladder Disease	Condition of Pancreas	Operation	Complications	Results	Comment
Acute c... cystitis ... cholelit...	...p. 101 ...e 122 ...p. 24	+	+	Gallstones	Hemorrhagic necrosis and edema	Cholecystectomy; choledochostomy; drain to lesser sac and gallbladder bed of liver; capsule of pancreas split and drained	None	Well	Slow onset; pain gradually increased in intensity; pathologic report of chronic cholecystitis
Acute c... cystitis ... common ... obstruc... by ston...	...p. 100.6 ...e 96 ...p. 22	0	+	Cholangeitis and gallstones	Hemorrhagic necrosis and edema	Cholecystectomy; choledochostomy; drain to lesser sac and gallbladder bed of liver; capsule of pancreas split and drained	None	Well	Sudden onset; marked edema of pancreas; inflammation of common duct with marked enlargement; pathologic report of acute cholecystitis
Acute c... cystitis	...p. 101 ...e 86 ...p. 22	+	0	Calculi in gallbladder and common duct	Hemorrhagic necrosis	Cholecystectomy; choledochostomy; drain to lesser sac; capsule of pancreas split and drained	None	Well	Sudden onset; incomplete common duct obstruction by calculi; entire pancreas hemorrhagic with beginning necrosis; pathologic report of chronic cholecystitis
Acute p... creatiti...	...p. 99.6 ...e 84 ...p. 24	+	0	Chronic cholecystitis and cholangeitis	Edema	Cholecystectomy; choledochostomy; drain to lesser sac; capsule of pancreas split and drained	Intra-abdominal collection	Well	Sudden onset; marked edema of pancreas; marked inflammation and dilatation of common duct; pathologic report of chronic cholecystitis
Perfora... gastric ... or acute ... pancrea...	...p. 99.8 ...e 90 ...p. 28	+	+	Edema of gallbladder wall	Hemorrhagic necrosis	Cholecystostomy; capsule of pancreas split and drained	Evisceration on 3d day following an asthmatic attack	Death within 4 days	Sudden onset; had severe asthmatic attacks in spite of medication; sat up in bed during violent seizure and evisceration occurred; died of generalized peritonitis and cardiac insufficiency
Acute c... cystitis	...p. 99.8 ...e 88 ...p. 20	+	+	0	Hemorrhagic necrosis and edema	Cholecystostomy; gauze drain to gallbladder and under surface of liver; capsule of pancreas split and drained	Generalized peritonitis and paralytic ileus	Death within 4 days	Sudden onset; pancreas markedly enlarged, filling entire upper part of the abdomen, and entirely necrotic from head to tail
Acute p... creatiti...	...p. 101 ...e 92 ...p. 24	+	+	Chronic cholecystitis with cholelithiasis	Hemorrhagic necrosis and edema	Cholecystectomy; choledochostomy; drain to lesser sac and gallbladder bed of liver; capsule of pancreas split and drained	Generalized peritonitis and paralytic ileus; cardiac insufficiency	Death within 5 days	Sudden onset; pancreas large and necrotic, especially the head; pain was colicky; pathologic report of chronic cholecystitis
Acute c... cystitis ... cholelit...	...p. 101 ...e 88 ...p. 20	0	+	Gallstones	Hemorrhagic necrosis and edema	Cholecystectomy; choledochostomy; drain to lesser sac; capsule of pancreas split and drained	None	Well	Slow onset; pain gradually increased in intensity; pathologic report of acute cholecystitis; electrocardiogram showed definite coronary disease
Acute p... atitis a... panied ... common ... obstruc... by calc... cholang...	...p. 100.6 ...e 116 ...p. 24	+	0	Cholangeitis and (3) common duct calculi	Hemorrhagic necrosis and edema	Choledochostomy with removal of calculi; drain to lesser capsule of pancreas split and drained	None	Well	Sudden onset of severe pain which was constant and only relieved by morphine; edema of gastrohepatic omentum and common duct

...as was pa...

...mononucle...

there was apparent involvement. The remainder showed various pathologic disturbances of the gallbladder or the bile ducts. Cholecystitis with concomitant cholelithiasis occurred in 54.54 per cent of the cases; cholecystitis, in 18.2 per cent, and choledocholithiasis per se in 9.09 per cent.

These operative observations, as well as the clinical symptoms in our series, lend emphasis to the experimental studies of the relationship of disease of the biliary tract to acute pancreatitis. The prevalent opinion as expressed by various reviews is to the effect that acute pancreatitis is usually secondary to an involvement of the biliary tract, as a result of which there may occur an intrapancreatic activation of trypsinogen and a subsequent autodigestion of the gland. The exact mechanism is still problematic.

DIAGNOSIS

From the foregoing it is obvious that the diagnosis can be made fairly easily in the case presenting an acute onset of knifelike pain in the epigastrium associated with prostration and cyanosis. In ten instances in which pain was localized in the epigastrium, seven patients had an associated shock and cyanosis. The character of the pain is similar to that occurring in a perforated gastric ulcer and hence may be mistaken for it even in the presence of prostration and cyanosis. This diagnosis was made in two of our cases because of an indefinite previous history suggesting gastric ulcer. Hence an adequate past history is of great importance. A less fulminating onset was presented in 36.36 per cent of our cases. It is noteworthy that in thirteen cases improperly diagnosed because of the absence of the typical picture of acute pancreatitis the patients were less than 40 years of age. As shown in the table, the average age in our group was 38.26 years; 63.64 per cent of the patients were less than 35 years of age. Although slightly lower than that reported in the literature, the age incidence generally agrees with that reported by others. In our cases the symptomatology indicated an involvement of the biliary tract. The suggestion is therefore made that for every patient, however young, in whom symptoms indicating an exacerbation of inflammation of the biliary tract is encountered, acute pancreatitis may be the causative factor. This is especially noteworthy when the patient is a male, since acute pancreatitis is just as frequent in males as in females, in contradistinction to the higher incidence of disease of the biliary tract in the latter.

PROGNOSIS

The prognosis of a case of acute pancreatitis is generally considered to be grave. Table 2 summarizes the available mortality data previously reported and those in our series. Obviously, many factors may be instrumental in affecting the mortality rate. Some investigators have

stated the belief that conservative treatment will increase the mortality; others, that the reverse is true. In one thousand two hundred and seventy eight patients with pancreatitis treated surgically, Schmieden and Sebening [4] reported a mortality rate of 51.2 per cent. A similar death rate was reported by McWhorter.[2] De Takáts and Mackenzie [1] reported a death rate of 36.6 per cent. Our series showed a mortality rate of only 22.7 per cent. Of the five patients who died postoperatively, two were practically moribund at the time of operation. Another patient (case 18), a man, aged 78, suffered from severe asthmatic seizures. For the first two days following operation the patient was in a fairly good condition. On the third day he had a severe asthmatic attack, during which evisceration occurred, he died within twenty-four hours.

TABLE 2.—*Mortality Data in Cases Previously Reported as Compared with Present Series*

Author	Year	Number of Cases	Mortality, per Cent
Broeq	Before 1910	116	78
	After 1910	119	66
Korte	1911	108	60
Guleke	1924	437	52.2
Schmieden and Sebening	1927	1,278	51.2
de Takáts and Mackenzie	1932	30	36.6
McWhorter	1932	64	54.7*
Koster and Kasman	1933	22	22.7

* Six not operated on, who died.

Two of the more important factors in determining the mortality rate are the severity of the disease and the degree of involvement of the pancreas. We have seen cases in which there was slight edema of the pancreas with slight enlargement and comparatively little necrosis and other cases in which the pancreas was so swollen and edematous that it filled the greater portion of the upper part of the abdominal cavity. In one instance a gland was encountered, the diameter of which in the sagittal plane of the body was 15 cm. Extreme degrees of necrosis involving the entire gland may also be encountered. Between these extremes are all degrees or gradations of severity, and obviously the clinical course varies with the degree and severity of involvement.

We feel definitely that early operation is indicated in all instances in which a diagnosis is made. This is true not only because we believe that the disease can be favorably influenced by operation at an early time but because of the difficulty in accurately making the diagnosis. Pancreatitis may be confused with some diseases in which operation is imperative, such as perforated ulcer.

4. Schmieden, V., and Sebening, W.: Arch. f. klin. Chir. **148**:319, 1927.

Although we recognize that the value of many of the other procedures combined in what we believe is the radical method of treating this disease may still be open to question, there can be little doubt regarding the favorable influence of decompression of biliary tension by drainage of the biliary tract, and we feel that the earlier this is instituted, the greater will be the likelihood of a favorable termination.

TREATMENT

We feel that the surgical treatment of acute hemorrhagic pancreatic inflammation must include the following steps: drainage of the biliary tract; removal of the gallbladder if it is diseased or contains stones; removal of calculi, if present, from the common duct; mobility of the duodenum by the Kocher method for the purpose of more accurately palpating the head of the pancreas in search of calculi in Wirsung's duct; splitting of the capsule of the pancreas for the relief of edema, and drainage of the lesser peritoneal sac and the pancreas. The drainage of the biliary tract is best accomplished: (1) by passing a rubber tube into the common bile duct through the stump of the cystic duct if the gallbladder has been removed for existing disease; (2) by passing a T-tube into the common duct, if it has been opened for the removal of stones, or (3) by a cholecystostomy in the absence of disease of the gallbladder or if, as occasionally occurs, the pancreas is so tremendously swollen as to make the common duct inaccessible. This type of complete operation was carried out in all of the cases in this series, with the exception of case 1, in which the patient was operated on before the procedure was adopted as routine, and cases 2 and 9, in which the patients were moribund on admission and in which it was deemed advisable simply to drain the pancreas. Cholecystostomies were performed on two patients (cases 18 and 19) for the purpose of instituting drainage of the biliary tract. In fifteen of the remaining seventeen patients cholecystectomies were performed with choledochostomy drainage through the stump of the cystic duct or directly by incision into the common bile duct, and in two of the cases (6 and 22) in which the gallbladder was removed previously, drainage was instituted through an incision in the common bile duct, and in each case three calculi of the common bile duct were removed. The operative procedure was carried out as follows:

After laparotomy the gallbladder and bile ducts were carefully examined. In the presence of cholelithiasis and cholecystitis the gallbladder was removed, preferably from below upward, and a catheter was passed into the common bile duct through the stump of the cystic duct and fixed in that position. If the aperature of the cystic duct was too small, the common bile duct was incised, a T-tube introduced directly and the cystic duct stump ligated. If it was deemed unnecessary to remove the gallbladder, the common duct was incised, and a T-tube drainage was instituted, after careful examination had been made to make

certain that no calculi were contained in it or after calculi had been removed. Then the peritoneum to the outer side of the duodenum was bluntly torn; the duodenum was rolled inward toward the median line and the head of the pancreas was exposed retroduodenally. This was carefully palpated for evidence of stone in the duct of Wirsung. If any was found it was removed; if none was found, the gastrohepatic omentum was incised, through which the pancreas was exposed; the capsule of the gland was slit longitudinally, and drainage over the gland was instituted by a cigaret drain or a gauze tamponade, depending on the condition of the pancreas. A cigaret drain was introduced into the lesser sac through the foramen of Winslow, and the abdomen was then closed.

SUMMARY AND CONCLUSION

Twenty-two cases of acute pancreatitis with a total mortality rate of 22.7 per cent are reported. Seven of the cases presented the typical picture of a sudden onset of severe epigastric pain followed by continual vomiting and associated with prostration and cyanosis. In two cases presenting a similar picture there was an indefinite previous history of a condition simulating gastric ulcer, which was diagnosed as such. In another case diagnosed as acute pancreatitis accompanied by obstruction of the common duct by calculi and cholangeitis of two weeks' duration there was no shock or cyanosis, but the patient was deeply jaundiced. The remainder of the cases presented a less precipitous onset, which was suggestive of acute disease of the biliary tract. Attention is drawn to the fact that this last-mentioned group of cases occurred most commonly in persons under 36 years of age. It is suggested that in making the diagnosis, acute pancreatitis should be suspected in every case which presents a history and symptomatology suggesting an acute exacerbation of disease of the biliary tract. Immediate and complete operation, which includes cholecystectomy if the gallbladder is diseased or contains calculi, probing of the ducts to assure freedom from calculi or to allow for their recognition and removal, drainage of the biliary tract and examination of Wirsung's duct, in addition to treatment of the pancreatic lesion and the associated peritonitis, is advocated.

CEREBRAL BLOOD FLOW: III AND IV

COBB PILCHER, M.D.
AND
CHARLES THUSS, M.D.
NASHVILLE, TENN.

III. CEREBRAL EFFECTS OF OCCLUSION OF THE COMMON OR INTERNAL CAROTID ARTERIES

The efficacy of the circle of Willis in establishing an adequate collateral circulation following occlusion of one of the internal or common carotid arteries has long been a matter of dispute. Advocated as a relatively harmless procedure by some authors, ligation of the carotid artery has been regarded by many others as an extremely hazardous operation, to be undertaken, if at all, in only the most desperate circumstances. One has only to read the following directly contradictory quotations from two eminent American surgeons to appreciate how widely divergent are the opinions on this subject:

Rudolph Matas,[1] in 1911, wrote: "A long and abundant experience with the surgery of the carotid artery, amounting in a period of twenty-five years to over seventy-eight ligations and extirpations of the common trunk and its two branches, has fully convinced me that the risk of fatal intracranial and cerebral complications resulting from an insufficient collateral circulation is not to be underestimated."

On the other hand, Harvey Cushing[2] said: "I have ligated the internal carotid many times without apparent symptoms. I don't now recall any accidents, but there may have been some. I have been careful to restrict these ligations to young or middle-aged persons without vascular disease. . . . Ligation of the common carotid has little, if any, effect on the circulation of head and brain, as anastomoses between the two external carotids are surprisingly free."

Such discrepancies in opinion, which might be multiplied many times from the literature, suggest the need of a critical analytic review of the subject.

From the Department of Surgery, Vanderbilt University School of Medicine.

1. Matas, R.: Testing the Efficiency of the Collateral Circulation as a Preliminary to the Occlusion of the Great Surgical Arteries, Ann. Surg. **53**:1, 1911.

2. Cushing, H.: Personal communication to the authors, Aug. 6, 1932.

THE LITERATURE

The literature, particularly of the nineteenth century, abounds in isolated reports of cases of ligation of the carotid artery. Scarcely a volume of the older journals can be examined without finding several. For a long period it was apparently the fashion to publish brief notes on single unusual cases, or to mention them in discussion of the articles of others. In most reports on carotid ligation no mention was made of cerebral complications. Of those which refer to associated cerebral conditions, many are so brief as to make the nature, or even the existence, of a cerebral disorder extremely doubtful. Furthermore, in pre-Listerian days, inevitable infection, with secondary hemorrhage, embolic complications and widespread constitutional phenomena, often added further confusion to the picture.

Fortunately, however, several excellent reviews of that period presented sufficient numbers of cases of ligation of the carotid artery to make a detailed review of most of the early cases unnecessary for the purposes of this article.

According to Garrison,[3] the use of the ligature was first described by Heliodorus (about 100 A. D.) and, shortly thereafter, by Archigenes and Antyllus, the latter describing the proximal and distal ligature for aneurysm which still bears his name.

Although the ancients (as claimed by Chevers,[4] in 1845) must have had occasion sometimes to tie the carotid arteries for hemorrhage, they avoided these vessels whenever possible.[5] We are not aware of a specific account of carotid occlusion until relatively modern times.

In 1765, Jean-Louis Petit [6] described a patient in whom an aneurysm of the right carotid artery had undergone spontaneous healing. The patient apparently had no neurologic symptoms, and died seven years later of apoplexy. The aneurysmal sac was completely obliterated. Baillie [7] described a similar case in 1793, and in the same year, according

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3. Garrison, F. H.: History of Medicine, ed. 2, Philadelphia, W. B. Saunders Company, 1917, p. 94. Neuberger, M., and Pagel, J.: Handbuch des Geschichte der Medizin, Jena, Gustav Fischer, 1902, vol. 1, pp. 365 and 488.

4. Chevers, Norman: Effects of Obliteration of the Carotid Arteries on the Cerebral Circulation, London M. Gaz. **1**:1140, 1845.

5. Paulus Aegineta: The Seven Books of Paulus Aegineta, translated by Francis Adams, London, The Sydenham Society, 1846, vol. 2, p. 311; translator's commentary, ibid. p. 312. Chirurgie de Paul d'Egine, translated by René Brian, Paris, Victor Masson, 1855, p. 181.

6. Petit, Jean-Louis, cited by Cutter.[8]

7. Baillie, Matthew: Tr. Soc. Improvement Med. & Chir. Knowledge, 1793, p. 122, cited by Cutter.[8]

to Cutter,[8] Hebenstreit[9] mentioned a case in which "the carotid artery was wounded during an operation for the removal of a tumor. The operating surgeon immediately tied the vessel and the patient lived for many years thereafter."

John Abernethy, of St. Bartholomew's Hospital, London, deserves credit for the first adequate description of a ligation of the common carotid artery. Some doubt exists as to the exact date of his operation. The date was given as 1798 by Cutter[8] and Garrison[10] and as 1803 by Pilz[11]; none was given by Norris.[12] Cutter and Pilz referred to the same publication[13] by Abernethy, while Norris referred to a different one.[14] The case was also reported in a later treatise[15] (1811), the only one available to us, but no date was given for the operation. Abernethy's report is very complete and shows careful observation of, and sane reflection on, the patient's condition. The patient had been gored in the neck by an ox, with resulting laceration of the left internal carotid artery and profuse hemorrhage. The common carotid artery was ligated. There developed paralysis of the right side and frequent convulsions on the left side, and the patient died thirty hours after the operation. Postmortem examination revealed extensive "inflammation" of the brain, with "injection" of the vessels and "light brown" cerebrospinal fluid.[16]

In 1803, the common carotid artery was ligated by Fleming,[17] in

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8. Cutter, I. S.: Ligation of the Common Carotid: Amos Twitchell, Surg., Gynec. & Obst. (Internat. Abstr. Surg.) **48**:1, 1929.

9. Hebenstreit, E. B. G.: Zusätze zu Benjamin Bell's Abhandlung von den Geschwüren und deren Behandlung, Leipzig, Weidmann, 1793.

10. Garrison,[8] p. 345.

11. Pilz, C.: Zur Ligatur des Arteria Carotis communis, Arch. f. klin. Chir. **9**:257, 1868.

12. Norris, N. W.: Statistics of the Mortality Following the Operation of Tying the Carotid Arteries and Arteria Innominata, Am. J. M. Sc. **14**:13 (July) 1847.

13. Abernethy, J.: Surgical Observations, London, T. N. Longman & O. Rees, 1804, p. 193.

14. Abernethy, J.: Surgical and Physiological Work, London, Rees, Arme, Brown and Green, 1830, vol. 2.

15. Abernethy, J.: Surgical Observations on Injuries of the Head, Philadelphia, Thomas Dobson, 1811, p. 72. It seems probable that this publication is simply an American edition (perhaps revised) of the treatise referred to by Cutter[8] and Pilz,[11] since the quotation made by Cutter appears verbatim in the American publication.

16. Abernethy's shrewd remarks on this case demonstrate an excellent knowledge of cerebral physiology. For example, he wrote with curiosity: "An effusion of blood in the left hemisphere of the brain would affect the opposite side of the body in the same manner that cutting off the supply of blood to the left side appears in this instance to have done" (p. 81).

17. Fleming: Med.-Chir. Rev. **3**:2, 1827.

England, for hemorrhage, and by Cogswell,[18] in America, in the course of removal of a tumor of the neck. The former's patient lived; the latter's died on the twentieth day, of secondary hemorrhage. Apparently neither patient showed cerebral symptoms.

In 1805, Sir Astley Cooper [19] first ligated the common carotid artery for aneurysm. Hemiparesis developed on the eighth day, and the patient died on the twenty-first day of "inflammation of the sac." The operation was repeated successfully (i. e., the patient survived), and without apparent cerebral symptoms, by Bjerkén [20] in 1807, this time for aneurysm behind the ear, and within a few days of that time, Twitchell [21] tied the common carotid artery for secondary hemorrhage following a gunshot wound. In 1808, Cooper [22] again operated for aneurysm of the common carotid artery, and this time the ligation was successful; the patient recovered, seemingly without complication, and died thirteen years later of apoplexy.

Valentine Mott,[23] in 1818, first ligated the innominate artery, and he ligated the common carotid artery many times in his long and active career.[24] His most important contribution, however, was the application of experimental principles to the subject. In 1831, he reported a careful anatomic study of the injected cervical vessels of a patient in whom one common carotid artery had been ligated three and a half months previously.[25] It is surprising that he failed to mention the intracranial circulation.

In the meantime, another interesting use of ligation of the carotid artery had been proposed and tested. In 1822, Boileau [26] tied one common carotid artery for hemorrhage in a patient known to have epilepsy, and observed that the convulsions ceased "for a considerable time."

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18. Cogswell, M. F.: New England J. Med. & Surg. **13**:357, 1824.

19. Cooper, Astley: A Case of Aneurysm of the Carotid Artery, Med.-Chir. Tr. **1**:1, 1812.

20. Bjerkén, cited by Pilz.[11]

21. Twitchell, Amos: Gunshot Wound of the Face and Neck; Ligature of the Carotid Artery, New England Quart. J. Med. **1**:188, 1843.

22. Cooper, Astley: Second Case of Carotid Aneurysm, Med.-Chir. Tr. London **1**:222, 1812; Account of the First Successful Operation Performed on the Common Carotid Artery, for Aneurysm, in the Year 1808, with the Post-Mortem Examination, in 1821, Guy's Hosp. Rep. **1**:53, 1836.

23. Mott, Valentine, cited by Burns: Successful Ligation of the Innominate Artery, J. A. M. A. **51**:1671 (Nov. 14) 1908, and by Norris,[12] p. 38. The latter also stated that the second innominate ligation was by von Graefe, in 1822, and cited other early ligations.

24. For detailed references to many of these cases, see the reviews of Norris [12] and Pilz.[11]

25. Mott, Valentine: Description of the Circulation of the Head and Neck in a Case After One Carotid Artery Had Been Tied, Am. J. M. Sc. **8**:45, 1831.

26. Boileau, cited by Norris,[12] p. 32.

Shortly thereafter, McClellan [27] tied the common carotid artery in 1 patient, Becton [28] in 1, and Preston [29] in 5 patients with "epilepsy," or similar neurologic complaints.[30] Subsequently, until after the middle of the century, carotid ligation was employed in many cases of various neurologic disorders, including trigeminal neuralgia, for which the first carotid ligation was done in 1817 by Liston.[31] In 2 of Preston's cases, both common carotid arteries were ligated, a procedure first carried out by Macgill,[32] in 1823.

In the middle third of the nineteenth century, a more critical attitude began to be adopted. Those who affirmed and those who denied the danger of carotid ligation engaged in a spirited controversy, using both clinical and experimental evidence. Mayer [33] performed a series of experiments on six varieties of animals, and concluded that "ligation of a single carotid artery may occasionally derange much the circulation of the cerebral vessels." [33b] On the other hand, Sir Astley Cooper [34] reported a masterful series of experiments on dogs and rabbits, in which he clearly showed that ligature of one or even of both carotid arteries in these animals may cause no major neurologic symptoms, whereas the obstruction of only one vertebral artery almost inevitably results in serious symptoms such as stupor, paralysis, convulsions or disorientation. He made no specific claims of the existence of a similar situation in man, but one is led to think that such was his belief.

Both sides of this controversy were well summarized, in 1845, by Chevers [4] in the first of the notable reviews dealing with the subject. After discussing the experimental and clinical evidence, he expressed the belief that, while ligation of the common carotid artery might often be accomplished with impunity, nevertheless, it was a dangerous procedure which should be employed only if demanded to save the life of the patient: ". . . it would be far better for the surgeon to make up his mind to contend with an active hemorrhage than that he should

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27. McClellan: Am. M. Rev. & J. **3**:328, 1826, cited by Pilz,[11] p. 372. The operation was performed in May, 1826.

28. Becton, F. E: North Am. M. & S. J. **4**:88, 1827.

29. Preston, J. R.: Tr. M. & Phys. Soc. Calcutta **5**:345 and 359, 1831; **6**: 394, 396 and 409, 1832.

30. Several of these cases bear the unmistakable signs of intracranial tumors.

31. Liston, R.: Cases of Aneurysm, Edinburgh M. & S. J. **16**:66, 1820.

32. Macgill, cited by Norris,[12] p. 37.

33. Mayer: (*a*) Acta Acad. cæs. Leopold. Carol. nat. cur. **6**:2, 1831; (*b*) reviewed in Edinburgh M. & S. J. **43**:487, 1883.

34. Cooper, A.: Some Experiments and Observations on Tying the Carotid and Vertebral Arteries and the Pneumogastric, Phrenic and Sympathetic Nerves, Guy's Hosp. Rep. **1**:457, 1836.

submit his patient to the chance of fatal hemiplegia, even although he believed that chance to be a remote one."

Inman [35] had previously (1844) included in his tables on operative mortality 40 cases in which the carotid artery was ligated, but the first detailed review of the cases reported in the literature was by George W. Norris [12] of Philadelphia. He tabulated 149 cases of carotid ligation. Of that number, 54 patients died as the result of operation. Severe cerebral symptoms appeared early in 25 patients, later (after the third day) in 7. Thirteen died of cerebral involvement. The cerebral symptoms varied from transient hemiplegia to convulsions, coma and death. He included a discussion of 10 cases in which both common carotid arteries had been ligated. In 2 of these both arteries were ligated at the same operation, and both patients died within twenty-four hours. One of the others had severe cerebral symptoms. Included, also, was a discussion of the 9 reported cases in which, up to that time, the innominate artery had been ligated; all the patients had died of secondary hemorrhage. No mention of cerebral symptoms was made. Subscribing entirely to the opinion of Chevers, Norris stated, "Close examination of the cases recorded . . . shows that the operation of deligating the carotid has been too generally looked upon as one of comparatively little danger; an analysis of them proves that serious symptoms frequently follow the mere cutting off of the supply of blood to the brain through this vessel. . . ."

The dangers of carotid ligation were similarly urged by Guthrie [36] and brought out in the reviews of Ehrmann [37] (cerebral symptoms in 47 of 213 cases), Wood [38] (death from "hemiplegia" in 3 of 49 cases) and LeFort [39] (cerebral symptoms in seventy-three of 241 cases). In 1868 appeared the splendid review of Pilz,[11] who reported 586 cases of common carotid ligation, with an operative mortality of 38.5 per cent, and the appearance of cerebral symptoms in 32 per cent. In his lengthy discussion, he pointed out the danger, cited experimental evidence and concluded that the safety of the operation depends on the

35. Inman, Thomas: Tables of the Mortality After Operations, Lancet **2**:39, 1844.

36. Guthrie, G. J.: Commentaries on the Surgery of the War in Portugal, Spain, France and the Netherlands, ed. 6, Philadelphia, J. B. Lippincott Company, 1862; Lancet **2**:143, 1850.

37. Ehrmann, J.: Des effets produits sur l'encéphale par l'oblitération des vaisseaux, qui s'y distribuent, Paris, B. Ballière, 1860.

38. Wood, J. R.: Early History of Ligature of the Common Carotid Artery, with a Report of the Unpublished Operations in the City of New York, New York J. Med. **3**:1, 1857. Two cases are mentioned in this report which may possibly antedate that of Abernethy.

39. LeFort, L.: Gaz. hebd. de méd. **11**:27, 1864, cited by Pilz.[11]

adequacy of the collateral circulation through the circle of Willis: ". . . von der Integrität jener Strombahnen und dieses Verbindungskreises hängt das Leben, oder wenigstens die volle Gesundheit der Operierten ab" (. . . on the integrity of the channels and connecting circle depends the life, or at least the complete health of the patient).[40]

Eight years later, James Spence[41] wrote: "There is no fear of interrupting the circulation in the brain after ligature of the [common] carotid, though this was formerly considered a great danger. Both carotids may be tied, and yet the circulation will be carried on perfectly." In 1877, Toland[42] stated: "I have ligated the common and external carotids frequently and in every case successfully."

With the teachings of Lister and the advent of aseptic surgery, the operative mortality and the percentages of infection and of secondary hemorrhage all dropped immediately, but the incidence of cerebral complications following carotid ligation remained virtually unchanged. In 1881 and 1882, Weljaminow[43] reported the cases of 33 patients, all operated on with "antiseptic" technic in only 1 of whom cerebral symptoms developed. He also found 20 "antiseptic" operations in the literature without a fatality. Subsequently, however, in a contradictory report from the same clinic, Hagen-Torn[44] stated that 4 instead of 1 of Weljaminow's patients had "indirect brain symptoms." In 1884, after reviewing 800 cases of ligation of the common carotid artery, Friedländer[45] concluded that "er die Ligatur der Carotis zur 'Kupierung akuter und Besserung chronischer Entzündungen' versuchen will" (he [the surgeon] will try ligature of the carotid artery for the arrest of acute and improvement of chronic inflammation). In the same year, Riegner[46] reported a remarkable patient who had one common carotid artery ligated for aneurysm, only to return a year later with an aneurysm of the other. This, too, was ligated. The night of the operation the patient had contralateral hemiparesis which disappeared by morning.

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40. Pilz,[11] p. 414.

41. Spence, James: Lectures on Surgery, ed. 2, Edinburgh, Adam & Charles Black, 1876, vol. II, p. 483.

42. Toland, H. H.: Lectures on Practical Surgery, Philadelphia, Lindsay & Blakiston, 1877.

43. Weljaminow, N. A.: Ein-und-zwanzig Fälle von Unterbindung der Arteria Carotis Communis, Vrach **2**:749 and 771, 1881; Zwölf Fälle von Unterbindung der Carotis Communis, ibid. **3**:490, 1882; abstr., Zentralbl. f. Chir. **9**:787, 1882.

44. Hagen-Torn, O.: Nothwendige Bemerkungen zu den Artikeln über 33 Fälle von Unterbindung der Art. carotis communis von N. A. Weljaminow, Med. Vestnik, no. 51, 1883; abstr., Zentralbl. f. Chir. **11**:430, 1884.

45. Friedländer, J.: Ueber die Ligature der Carotis, Inaug. Dissert., Dorpat, 1881; abstr., Zentralbl. f. Chir. **11**:429, 1884.

46. Riegner, O.: Doppelseitiges Aneurysma der Carotis communis, durch Unterbindung beider Carotiden geheilt, Zentralbl. f. Chir. **11**:431, 1884.

In 1892, Zimmermann [47] collected 65 cases of ligation of the common carotid artery reported after 1880. Of these patients 31 per cent died and 26 per cent showed cerebral symptoms. Ten years later appeared Jacobsthal's two reviews [48] of the surgical treatment of aneurysms of the innominate and subclavian arteries, respectively. In both series, the innominate or common carotid arteries, or both, were ligated in 145 patients. Of these groups cerebral symptoms developed in 8. These figures have little significance, however, in view of the high immediate operative mortality. Jacobsthal, although he recognized the danger of cerebral complications, was inclined to minimize it: "Der Collateralkreislauf bildet sich meist so schnell und reichlich aus, dass Schädigungen in Folge ungenüngender Blutzufuhr zum Arm und Gehirn nur zelten auftreten" (the collateral circulation generally develops so rapidly and completely that changes resulting from insufficient blood supply to the arms and brain occur only rarely).[49] And again: "Der durch die Aeste der 1. carotis und subclavia, durch Vermittelung der r. Vertebralis und Subscapularis . . . hergestelle Kreislauf erweist sich als genügend." (The circulation formed by the branches of the first carotid and the subclavian arteries by way of the right vertebral and subscapsular arteries . . . proves sufficient).[50]

In 1908, Burns [51] reported 46 cases of ligation of the innominate artery. Of these patients, 6 died of "some cerebral lesion."

In 1906, there appeared the first of two opinions directly contradictory to each other, in the French literature. Savariaud,[52] in his review on subclavian aneurysms, stated: "La conclusion . . . c'est que la ligature . . . de la carotide, ou de la vertébrale . . . est une opération grave, très grave même, tant du fait . . . du voisinage des collatérales, qu'à cause des troubles cérébraux engendrés par ces ligatures." (The conclusion is that ligature of the carotid or of the vertebral artery is a serious, even a very serious operation, owing to the

47. Zimmermann, W.: Ueber die Gehirnerweichung nach Unterbindung der Carotis Communis, Beitr. z. klin. Chir. **8**:364, 1892.

48. Jacobsthal, H.: (*a*) Beiträge zur Statistik der operativ-behandelten Aneurysm: I. Das Aneurysma der Arteria anonyma, Deutsche Ztschr. f. Chir. **63**:550, 1902. (*b*) II. Das Aneurysma der Arteria Subclavia, ibid. **68**:239, 1903. Two cases of innominate aneurysm not included in the first review were reported by Page (Lancet **1**:1004, 1895) and by Ryan (ibid. **1**:1549, 1895). No mention of cerebral symptoms was made in either case.

49. Jacobsthal,[48b] p. 282.

50. Jacobsthal,[48a] p. 568.

51. Burns: Successful Ligation of the Innominate Artery, J. A. M. A. **51**:1671 (Nov. 14) 1908.

52. Savariaud, M.: Le traitement chirurgical des anévrismes de l'artère sousclavière, Rev. de chir., Paris **34**:1, 1906.

proximity of the collateral arteries and of the cerebral disturbances produced by these ligatures.)

Three years after this, Guinard,[53] after stating that he did not believe that either immediate or delayed cerebral complications follow ligation of the carotid artery low in the neck, if the opposite carotid artery and its branches are intact, added: "et alors si on se reporte aux cas de ligature carotidienne pour la cure des anévrysmes, c'est-a-dire chez des malades qui n'ont pas eu d'opérations sur la face, la langue ou le cou, il n'y avait pas d'example que le moindre accident cérébral imédiat ait été observé" (if one refers to cases of carotid ligature for the cure of aneurysms in patients who have not had operations on the face, the tongue or the neck, one will find no example of the slightest direct cerebral complication).

Such was the status of opinion when Matas, in 1911, gave the warning of danger quoted in the introduction of this article and when Halsted,[54] in 1914, first advocated the use of metal bands for partially occluding the artery to increase the collateral circulation. Since then, uncomplicated ligations of the common carotid arteries have been reported by Shipley and Lynn[55] (2 cases), Makins,[56] Bond and Mitchell,[57] Telford[58] and Bolt.[59] Griffiths[60] ligated both common carotid arteries without the production of cerebral symptoms. In 2 cases reported by Dandy,[61] it is uncertain whether the common or internal

53. Guinard, A.: Traitement des anévrysmes de la base du cou, Rev. de chir., Paris **39**:229, 1909.

54. Halsted, W. S.: Des partielle Verschluss grosser Arterien, Verhandl. d. deutsch. Gesellsch. f. Chir. **43**:349, 1914; Cylindrical Dilatation of the Common Carotid Artery Following Partial Occlusion of the Innominate and Ligation of the Subclavian, Surg., Gynec. & Obst. **27**:547, 1918.

55. Shipley, A. M., and Lynn, F. S.: Carotid Tumor and Aneurysm of the Internal Carotid, Report of Cases, J. A. M. A. **66**:1602 (May 20) 1916.

56. Makins, G. H.: On the Vascular Lesions Produced by Gunshot Injuries and Their Results, Brit. J. Surg. **3**:353, 1915.

57. Bond, C. J., and Mitchell: Arteriovenous Aneurysm of the Common Carotid Artery, Brit. J. Surg. **3**:307, 1915.

58. Telford, E. D.: Varicose Aneurysm of Left Common Carotid Artery and Internal Jugular Vein, Brit. J. Surg. **3**:322, 1915.

59. Bolt, R. F.: Aneurysm at the Termination of the External Carotid Artery and Aneurysmal Varix Between the Bifurcation of the Common Carotid Artery and the Internal Jugular Vein, Lancet **2**:1015, 1916.

60. Griffiths, C. A.: Hemorrhage from a Large Vessel in or About the Base of the Skull: Internal Ligature of Both Carotids, Brit. J. Surg. **3**:302, 1915. For other such cases, see Locke.[68]

61. Dandy, W. E.: Arteriovenous Aneurysm of the Brain, Arch. Surg. **17**: 190 (Aug.) 1928. In the text it is stated that the common carotid artery was ligated in both cases (IV and VIII), but in the tables, the internal carotid arteries are said to have been ligated.

carotid artery was ligated. Cerebral complications occurred after ligation of the common carotid artery by Makins,[56] by Madden [62] and by Bland-Sutton.[63]

In the experimental laboratory in recent years, Chauchard and Chauchard [64] studied the "chronaxie" after occlusion of common carotid and vertebral arteries. They found no change an hour and a half after all four vessels were occluded (in dogs). Houssay and Hug [65] found that the maximum period of toleration of complete ischemia of the dog's brain was from eleven to fifteen minutes. As reported later in this article, my colleague and I recently found only slight transient diminution in the volume of flow of blood through the dog's brain following occlusion of one common carotid artery.

The operation of ligation of the internal carotid artery has apparently been employed less frequently. It has been employed or suggested in the treatment of intracranial aneurysms and anomalous arteriovenous communications [66] and as a preliminary measure to extensive operative procedures in the field of its distribution (as in the case of Gluck [67]), but by far the most common condition for which it has been done is the pulsating exophthalmos due, in most cases, to an arteriovenous fistula between the internal carotid artery and the cavernous sinus. The treatment of this condition was admirably reviewed, in 1924, by Locke,[68] who summarized 588 cases, in 38 of which the patients were treated by ligation of the internal carotid artery. Twenty-one and five-hundredths per cent were "cured," 65.79 per cent "improved." Death occurred in 7.9 per cent. Locke advocates careful tests for the adequacy of the collateral circulation by preliminary temporary occlusion of the artery at or before operation (under local anesthesia). He

62. Madden, F. C.: A Case of Marked Temporary Aphasia After Ligature of the Common Carotid Artery for Traumatic Aneurysm, Brit. M. J. **1**:585, 1916.

63. Bland-Sutton, J.: An Aneurysmal Varix of the Internal Jugular Vein and Internal Carotid Artery with Unusual Complications, Brit. J. Surg. **3**:490, 1915.

64. Chauchard, A., and Chauchard, B.: Influence de la ligature des artères carotides et vertébrales sur l'excitabilité de l'écorce cérébrale, Compt. rend. Soc. de biol. **99**:1572, 1928.

65. Houssay, B. A., and Hug, E.: Action de l'anémie encéphalique sur les centres nerveux et vagaux cardiaques, gastriques et intestinaux de la tête isolée, Compt. rend. Soc. de biol. **99**:1503, 1928.

66. Cushing, H.: Contributions to the Clinical Study of Intracranial Aneurysms, Guy's Hosp. Rep. **73**:159, 1923. Dandy.[61].

67. Gluck: Ueber einen Fall von partiellen Resektion des Felsenbeinpyramide, nebst Bemerkungen über die Ligatur des Carotis interna in Canalis carotica, Verhandl. d. deutsch. Gesellsch. f. Chir. **9**:37, 1882.

68. Locke, C. E., Jr.: Intracranial Arteriovenous Aneurysm or Pulsating Exophthalmus, Ann. Surg. **80**:1, 1924. Included in this review are 258 cases of common carotid ligation and 21 cases of bilateral carotid ligation.

expressed the belief that if this is done the risk of cerebral anemia is negligible, but that without such tests, ligation of the common carotid artery is preferable (mortality, 1.28 per cent in his series). Dandy[69] recently stated: "This condition (arteriovenous aneurysm between the internal carotid and the cavernous sinus and its sequelae) is easily cured by either partial or complete ligation of the internal carotid artery. After the age of 35, total ligation of the artery is dangerous. A partial occlusion of the artery with a band of fascia is just as effective as a complete ligation."

COMMENT

To compute accurate percentages of cerebral complications is impossible in view of the incompleteness of many reports and the possible

TABLE 1.—*Age Incidence of Cerebral Complications Following Ligation of the Common Carotid Artery*

Age	Ligation for Hemorrhage	Ligation for Aneurysm or Similar Lesion	Ligation for Other Reasons	Total
10 to 20	4	6	0	10
20 to 30	14	14	4	32
30 to 40	4	4	0	8
40 to 50	2	20	2	24
50 to 60	4	6	2	12
60 to 70	6	6	0	12
70 and over	0	2	0	2
Total	34	58	8	100

extraneous factors involved in many of the cases. From so large a mass of such variable material, conclusions may be drawn only with great care. However, it is certainly true that occlusion of a common carotid artery will be followed by definite symptoms referable to the brain in a considerable number of cases (probably from 20 to 30 per cent) and that occasionally these symptoms will be serious enough to leave permanent residual damage or, rarely, to produce death.

Certain factors might be expected to influence the frequency of cerebral complications. For example, one might suppose that such complications would occur with greater frequency in cases of advanced cerebral arteriosclerosis, in which the cerebral circulation may already be near its minimum threshold of adequacy and in which the cerebral vessels are able to respond but poorly to the demand for establishment of a collateral circulation, a supposition emphasized in 1908 by von

69. Dandy, W. E.: Diagnosis and Treatment of Injuries of the Head, J. A. M. A. **101**:772 (Sept. 2) 1933.

Oppel.[70] This does not prove to be the case, however. In table 1 is shown the age incidence in 100 cases selected at random from the literature in which definite cerebral symptoms occurred following ligation of one common carotid artery. It will be seen that in the majority of cases the patients were under 50 years of age, hence were probably not affected by advanced cerebral vascular disease. Further, if the cases of aneurysm, arteriovenous fistula and similar conditions are left out (for reasons given in the following paragraph), the incidence is far greater in young people. That young people are more liable to trauma is doubtless an important factor in the production of this high percentage.

In a person with an aneurysm of long standing or with similar local vascular disease a compensating collateral circulation might be expected already to have developed, thus making him less liable to cerebral complication if the carotid artery is ligated. But in the 259 cases with preexisting aneurysms or similar lesions reported by Pilz cerebral complications developed in 75 (29 per cent), a figure surprisingly close to the incidence of 32 per cent for his whole series.

There are, then, no criteria on which to base a preoperative prognosis. Danger apparently exists in all cases. The common (or internal) carotid artery should therefore be occluded only in cases in which a greater danger lies in permitting it to remain unoccluded.

IV. EFFECT OF OCCLUSION OF THE COMMON CAROTID ARTERIES ON THE VOLUME-FLOW OF BLOOD THROUGH THE DOG'S BRAIN

It is realized that final conclusions regarding man cannot be drawn from experimentation on animals alone, but the similarity of the cerebroarterial systems in man and the dog will at least allow the making of tentative assumptions. Houssay and Hug,[65] using the "isolated head" preparation, found the greatest time for which the brain might be entirely deprived of blood without loss of the ability to resume its function to be from eleven to fifteen minutes. On the other hand, Chauchard and Chauchard[64] found no difference in chronaxie after occlusion of both common carotid and both vertebral arteries. To our knowledge, no studies have been made on the direct effect on the cerebral circulation of occlusion of these vessels.

METHODS

Thirteen experiments were performed on dogs anesthetized by sodium barbital (0.3 Gm. per kilogram of body weight) given intravenously. Each experiment was begun from two to four hours after the injection of the barbital. The arterio-

70. von Oppel, W. A.: Zur operativen Behandlung der Arterio-venösen Aneurysmen, Arch. f. klin. Chir. **86**:32, 1908.

venous oxygen difference of blood flowing through the brain was determined by the method used in previous studies in this series.[71] The common carotid arteries (and, in some experiments, the vertebral arteries) were exposed and isolated by a midline anterior cervical incision, and were occluded when desired by means of rubber covered "bulldog" clips. Duplicate control determinations were made in all experiments. In nine experiments, one common carotid artery was then occluded, and in eight, another determination was made as quickly as possible afterward. The interval between the occlusion of the artery and the drawing of the samples of blood was usually less than three minutes and never more than five minutes. The venous sample was always drawn first. In seven experiments, subsequent determinations were made at intervals of from thirty to sixty minutes, and again after two hours in four experiments. In three of the experiments, the second common carotid artery was later occluded and the determinations repeated immediately and at longer intervals afterward.

TABLE 2.—*Effect of Occlusion of One and of Both Common Carotid Arteries*

	Determination	Time, Minutes	Arterial Oxygen Content, per Cent by Volume	Venous Oxygen Content, per Cent by Volume	Arteriovenous Oxygen Difference, per Cent by Volume	Change from Control, per Cent by Volume
Dog C₂: male; weight, 10.2 Kg.; sodium barbital 3 Gm. intravenously four hours before beginning experiment	I and II (Average)	...	12.90	9.93	2.97	.....
		29	Clip placed on right common carotid artery			
	III	30	12.96	8.12	4.84	+1.87
	IV	60	11.55	8.99	2.56	—0.41
	V	180	12.94	10.09	2.85	—0.12
		290	Clip placed on left common carotid artery			
	VI	295	13.17	7.57	5.60	+2.63
	VII	325	13.42	8.30	5.12	+2.15
	VIII	360	14.51	9.56	4.99	+2.02
	IX	870	12.84	7.15	5.69	+2.72

In four experiments, the effect of occlusion of the vertebral and common carotid arteries was studied, the vessels being occluded one at a time, and each occlusion being followed by a determination of the cerebral arteriovenous oxygen difference.

RESULTS

Effect of Occlusion of One Common Carotid Artery.—In seven of the nine experiments there was an immediate moderate increase in the arteriovenous oxygen difference (1.87, 3.66, 1.57, 1.65, 1.51, 1.27 and 2.40 per cent by volume, respectively); in one experiment there was a diminution of 0.72 per cent by volume. In the remaining experiment, no immediate determination was made. The average immediate change in the eight experiments was an increase of 1.65 per cent by volume. The values in a typical experiment are given in table 2.

71. Pilcher, C.: Cerebral Blood Flow: I. The Effect of Intravenous Administration of Hypertonic and Hypotonic Solutions on the Volume Flow of Blood Through the Brain, Arch. Neurol. & Psychiat. **24**:899 (Nov.) 1930. Hamm, L., and Pilcher, C.: Cerebral Blood Flow: II. The Effect of Intravenous Injection of Hypertonic and Hypotonic Solutions on the Cardiac Output and Blood Pressure, ibid. **24**:907 (Nov.) 1930.

In all seven determinations done from thirty to sixty minutes after occlusion of the artery, the direction of change was toward the control level, and in five of the seven the values may be said to have returned to normal (+0.12, +0.16, —0.49, —0.41 and —0.10 per cent by volume, respectively). In the remaining two, values of +1.22 and +1.05 per cent by volume were found, as opposed to +3.66 and

TABLE 3.—*Effect of Occlusion of the Second Common Carotid Artery*

Dog	Time Following Occlusion of Second Carotid, Minutes	Change from Control, per Cent by Volume	Change from Last Determination Before Occlusion of Second Carotid, per Cent by Volume
C_3	5	+2.63	+2.75
	35	+2.15	+2.27
	70	+2.02	+2.14
	580	+2.72	+2.84
C_4	1	+0.96	+0.84
	30	+4.08	+3.96
C_5	5	+2.40	±0.00
	50	+4.10	+1.70

TABLE 4.—*Effect of Occlusion of Each Vertebral and Carotid Artery in Series*

Determination	Time, Minutes	Arterial Oxygen Content, per Cent by Volume	Venous Oxygen Content, per Cent by Volume	Arteriovenous Oxygen Difference, per Cent by Volume	Change from Control, per Cent by Volume
I and II (Average)	..	17.16	12.48	4.68	.....
	20	Clip placed on left vertebral artery			
III	30	16.40	11.70	4.70	+0.02
	35	Clip placed on left common carotid artery			
IV	45	16.40	10.55	5.85	+1.17
	50	Clip placed on right vertebral artery			
V	60	16.29	10.61	5.68	+1.00
	65	Clip placed on right common carotid artery			
VI	75	16.71	8.53	8.18	+3.50
	85	All clips removed			
VII	95	15.70	11.21	4.49	—0.19

+1.65 per cent by volume, respectively, immediately after occlusion of the artery. Again, in three of the four determinations made two hours after occlusion of the artery, the arteriovenous oxygen difference was within the limits of normal (+0.97, —0.24 and —0.12 per cent by volume respectively). In the fourth, the value was +2.66 per cent by volume (it had been +1.65 at one minute and +1.05 per cent by volume at thirty minutes after occlusion of the artery). The reason for the increase in utilization of oxygen is not apparent. The mean blood pressure, which was recorded in this experiment, had already risen slowly from a control level of 120 mm. of mercury to 140 mm. at the time of the last determination.

To summarize, occlusion of one common carotid artery resulted usually in an immediate moderate increase in arteriovenous oxygen difference, followed by a fairly rapid return toward, or even slightly below the normal level. Here it was usually maintained for the two hours during which the determinations were made.

Effect of Subsequent Occlusion of the Second Common Carotid Artery.—The results are summarized in table 3 and the detailed results in one experiment are given in table 2. Immediately following occlusion of the second carotid artery there was a definite increase in arteriovenous oxygen difference in one experiment and little or no change in the other two. However, later determinations showed a marked and sustained increase.

Effect of Occlusion of Both Carotid and Both Vertebral Arteries.—The four experiments gave identical results qualitatively, and the changes closely approximated each other quantitatively. The detailed results in one are given in table 4. Occlusion of one vertebral artery resulted in no appreciable change, but occlusion of one carotid artery was followed by a definite increase in the arteriovenous oxygen difference. Again, occlusion of the second vertebral artery caused little or no change, but when a clip was placed on the second common carotid artery, there was always a marked increase. When all the clips were removed, the arteriovenous oxygen difference returned to a normal or slightly subnormal level.

CONCLUSIONS

It must be remembered that any interpretation of the results of these experiments in terms of volume of flow of blood depends on the assumption of a constant consumption of oxygen by the brain throughout the experiments. If the consumption of oxygen is constant, the volume of flow will vary inversely as the arteriovenous oxygen difference. Although there is no reason to believe that the consumption of oxygen of the brain will vary during such experiments, such an assumption must, nevertheless, be purely a tentative one.

If this is borne in mind, it is justifiable to conclude that these experiments indicate the following:

1. Occlusion of one common carotid artery of the dog causes a temporary decrease in the volume of flow of blood through the brain, but this decrease is quickly compensated for, largely, no doubt, through the collateral pathways of the circle of Willis.

2. Occlusion of both common carotid arteries of the dog results in a sustained diminution in the volume of flow of blood through the brain.

3. Occlusion of the vertebral arteries of the dog has comparatively little effect on the cerebral blood flow.

ABSORPTION OF DEXTROSE FROM THE COLON

W. W. EBELING, M.D.*
PHILADELPHIA

Within the past few years McNealy and Willems,[1] Pressman,[2] Scott and Zweighaft,[3] Perusse,[4] Burget, Moore and Lloyd[5] and Collens and Boas[6] published data on the absorption of dextrose from the colon which are not entirely in agreement. The subject is of sufficient importance from the clinical point of view to warrant additional studies.

I reported[7] the results of studies on the absorption of dextrose from the colon of the anesthetized dog. It was assumed at that time that anesthesia and the attending operation played little or no part in altering the physiologic process of absorption from the large intestine.

The opportunity arose, however, to study absorption from the colon in the unanesthetized dog through the preparation of a colon loop. One need not, at this time, comment on the advantages or disadvantages of the use of the chronic loop for investigation of intestinal absorption. The results of the studies of Ravdin and his associates[8] on chronic jejunal loops, as well as the results obtained in these experiments, are sufficiently consistent to permit one to conclude that from the chronic loop results may be obtained from which deductions may be drawn as to the activity of the intestinal mucosa. The closed colon loop is comparable to the colon under normal circumstances, in which one end is closed by the rectal sphincters and the other by the ileocecal valve.

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* Hunter Fellow in Surgery.

From the Laboratory of Research Surgery and the Department of Surgery (Division C), University of Pennsylvania.

1. McNealy, R. W., and Willems, J. D.: Absorption of Dextrose from Colon: Study of Effects of Chemical Excitants and of Stimulants on Dextrose Enema, Arch. Surg. **22**:649 (April) 1931.

2. Pressman, J. J.: Am. J. M. Sc. **179**:520, 1930.

3. Scott, E. L., and Zweighaft, J. F. B.: Blood Sugar in Man Following Rectal Administration of Dextrose, Arch. Int. Med. **49**:221 (Feb.) 1932.

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5. Burget, G. E.; Moore, P. H., and Lloyd, R. W.: Am. J. Physiol. **105**: 187, 1933.

6. Collens, W. S., and Boas, L. C.: Arch. Int. Med. **52**:317 (Aug.) 1933.

7. Ebeling, W. W.: Absorption of Dextrose from Colon, Arch. Surg. **26**: 134 (Jan.) 1933.

8. Ravdin, I. S.; Johnston, C. G., and Morrison, P. J.: Am. J. Physiol. **194**: 700, 1933.

METHOD

Preparation of a Chronic Colon Loop.—The dogs selected for these experiments were of mongrel breeds and weighed from 12 to 20 Kg. The successful preparation of the chronic loop was obtained by a two-stage operation done under aseptic technic. The anesthetic employed for the operation was ether, administered by the open drop method.

The first stage consisted of a midline laparotomy incision, following which the terminal part of the ileum and the cecum, with its attached appendix, were mobilized. A point approximately 4 or 5 cm. from the ileocecal valve was selected for transection of the ileum. The point of transection of the terminal part of the ileum depended primarily on the arrangement of the vascular supply to that portion of the intestine. The division was usually made midway between two of the larger terminal branches of the mesenteric artery. The reason for this care is that the stump of the ileum, which remains attached to the cecum, depends on the blood supply from the mesenteric vessels rather than on that from the colic branches.

The ileum was divided with the actual cautery between two obstructing ligatures of silk. The two raw ends of the ileum resulting from this transection were then buried by means of purse-string sutures of Pagenstecher. The stumps were reenforced by one or two through-and-through seromuscular sutures of similar material. It was often necessary to free the attachment of the appendix alongside the terminal part of the ileum before closure of the distal stump could be completed.

The cecum, with its attached appendix and small stump of ileum, was then allowed to drop back within the abdominal cavity, following which an anastomosis between the ileum and the lower sigmoid flexure was made.

The anastomosis of the terminal part of the ileum to the lower sigmoid flexure was of the side-to-side type and was placed as low on the sigmoid flexure or upper part of the rectum as possible. Anastomotic clamps were employed merely to obstruct the enteric flow in the ileum, and likewise to obstruct the fecal current in the sigmoid flexure during the anastomotic procedure, the contents of the intestine having been milked out prior to the application of the rubber-covered clamps. The incisions in the side of the ileum and sigmoid flexure usually measured about 3 cm. The anastomosis was completed with a double row of fine Pagenstecher sutures, the serosal surfaces being additionally reenforced with occasional interrupted sutures of fine black silk.

A number 12 to 14 soft rubber catheter was passed by an assistant through the anus into the rectum, and was fed through the anastomosis into the terminal part of the ileum to the extent of about 2 or 3 inches (2 or 7.6 cm.). From 6 to 8 inches (15 to 20 cm.) of rubber catheter usually sufficed to reach from the anal orifice up to and through the ileosigmoidostomy opening. From this one could readily determine how far down on the sigmoid flexure the anastomosis had been made.

The abdomen was then closed in layers. Two hundred and fifty cubic centimeters of salt solution was permitted to remain within the peritoneal cavity.

The rectal catheter was usually passed spontaneously after about twenty-four hours. Following immediate recovery, the dogs were returned to the animal house for convalescence before proceeding with the final construction of the colon loop. The animals had diarrhea which frequently persisted for a number of days. In the dogs that survived the initial operation for several weeks, semisoft and later formed stools finally made their appearance.

The mortality in this primary procedure was high, death resulting most frequently from interference with the blood supply of the terminal part of the ileum, owing to the torsion required to bring that portion of the ileum into contact with the lower sigmoid flexure. The dogs that survived this procedure remained apparently healthy, and one in particular, a small wire-haired terrier, gained weight to such an extent that he became rather fat.

The second stage was proceeded with in from three to six weeks following recovery from the primary operation. Laparotomy was performed through an incision of the left rectus muscle. It was surprising to note that in the dogs surviving the initial operation, there were few adhesions within the abdomen. The anastomosis in each instance was cleancut and well formed.

The sigmoid flexure, about 3 cm. proximal to the side of the anastomosis, was ligated at two levels with silk ligatures placed 1 cm. from one another. After the knots were tied down, the ends were permitted to remain long and were held by hemostats which enabled one to mobilize the sigmoid flexure with ease. The mesosigmoid was then carefully separated from its intestinal attachment, special care being taken to control hemostasis without obstructing the larger colic vessels. The sigmoid flexure was cut through with the actual cautery between the two obstructing ligatures, and the stumps were then buried with purse-strings of Pagenstecher. Seromuscular mattress sutures of Pagenstecher were employed to reenforce the closure. Both stumps were brought permanently end-to-end by means of the last placed mattress sutures, the long or free ends of which were used for this purpose.

The inversion of the stump of the distal part of the sigmoid flexure appeared to interfere with the actual anastomosis by somewhat filling the lumen of the sigmoid flexure; however, no difficulty was encountered in the convalescence of the animals from this intereference. The rent in the mesentery was not closed, and it appeared to be obliterated in a large part when the two blind ends of the sigmoid flexure were brought adjacent to one another.

The formation of a fistulous opening into the colon loop was carried out as follows: The short distal stump of ileum, which had been separated from the terminal part of the ileum and which had been left attached to the cecum, was brought out of the abdomen through a stab wound to the outer side of the right rectus muscle. Its position was maintained with four interrupted sutures of silk placed at the ends and sides of the stab wound and passed through the serosal and muscular layers of the protruding intestine. Two hundred and fifty cubic centimeters of salt solution was placed in the peritoneal cavity and the laparotomy incision was then closed in layers.

The stump of protruding ileum was opened after several days. The opening thus accomplished permitted ready entry into the colon loop. A small rubber tube measuring about 2 or 3 inches was passed into the colon loop through the enterostomy opening, and the colon loop was gently washed out with warm salt solution.

The rubber tube was permitted to remain in the enterostomy opening for from twenty-four to forty-eight hours, the loop being carefully washed out once or twice during that period, after which the tube was completely removed. The dogs were then returned to the animal house for convalescence. The colon loop was irrigated at frequent intervals during the convalescence and prior to the beginning of the absorption experiments. The animals used in these experiments appeared to remain quite healthy, and their wounds healed without complications.

Absorption experiments were conducted by the double balloon method described by Johnston[9] and used by Ravdin and his associates[8] in their studies on small intestinal loops. A number 14 French soft rubber catheter was perforated freely along that portion which was to lie within the intestinal loop. Two small rubber balloons were placed around this main catheter at a point corresponding to the abdominal wall when the main catheter lay within and throughout the extent of the chronic colon loop. When the two balloons were distended through their separate tubes, the one just within the abdominal loop prevented the catheter from coming out of the loop, while the second, just outside the abdominal wall, prevented the catheter from further entering the loop. Both balloons prevented the loss of fluid from the loop.

Throughout these studies, the dogs were given the routine laboratory diet. Absorption experiments were usually conducted in the afternoon, approximately eighteen hours after the last meal.

For each absorption experiment or series of experiments, the catheter with its balloon was inserted into the loop through the ileostomy opening and fixed in place by distention of the balloons. The loop was then carefully irrigated with warm water until all washings returned clear. It is to be noted that after from twenty-four to forty-eight hours of disuse, a considerable quantity of thick mucus could be washed from the loop. An abdominal binder was usually applied about the animal, through one point of which the end of the main catheter entering the loop protruded. By this method, it was possible quickly to introduce fluids into, or withdraw them from, the colon loop without disturbing the abdominal binder. The abdominal binders were necessary because of the desire of the dogs to chew the rubber catheters and balloons while these were in position.

All the dextrose solutions were freshly made from Bactodextrose. The concentration of the dextrose was determined in all instances by the Benedict method[10] immediately before and at the completion of each experiment.

A measured amount of dextrose solution to be used was introduced into the cleansed and empty loop. The soft rubber catheter, which extended to the end of the loop, was then closed with a Hoffman clamp. At the end of each experiment, the contents of the loop were withdrawn, measured and placed in a volumetric flask, and the loop was then washed out with sufficient water to make up the volume desired for analysis.

RESULTS

Three dogs were used for the experiments reported in this paper. Data obtained with the same concentrations of dextrose solution in the same dog were quite similar. While in each instance varying concentrations were not run in series (e. g., 5 per cent for the first hour, 10 per cent for the second hour and 25 per cent for the third hour), in all the experiments reported in this paper the different concentrations were run serially. It was found that there were minor variations for similar concentrations from day to day, although fundamentally, when compared with the changes which occurred with the higher concentrations, they were relatively insignificant.

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9. Johnston, G. G.: Proc. Soc. Exper. Biol. & Med. **30**:193, 1932.

10. Benedict, S. R.: The Detection and Estimation of Glucose in Urine, J. A. M. A. **57**:1193 (Oct. 7) 1911.

Effect of Varying the Concentration of Dextrose.—The experiments were planned to test the effect of concentration on the total amount of dextrose absorbed per unit of time. When the concentration was changed only a little, as from 1 to 2.5 per cent, the amount of dextrose absorbed from the 2.5 per cent solution was, as a rule, similar or only slightly higher than that absorbed from the 1 per cent solution. This was at times true with the change from a 2.5 per cent to a 5 per cent solution. The differences between slightly different concentrations were often not as great as those observed by Ravdin and his associates,[8] when a

TABLE 1.—*Effect of Varying the Concentration of Dextrose*

Dog	Date	Time, Hours	Volume In, Cc.	Volume Out, Cc.	Concentration In, Gm. per 100 Cc.	Concentration Out, Gm. per 100 Cc.	Total In, Mg.	Total Out, Mg.	Total Lost, Mg.
179	8/10/33	1	25	31	5.6	3.8	1,400	1,178	222
	8/10/33	1	25	49	11.2	5.0	2,800	2,450	350
	8/10/33	1	25	72	27.9	8.5	6,975	6,120	855
425	8/10/33	1	25	30	5.8	3.3	1,450	990	460
	8/10/33	1	25	50	11.6	4.3	2,900	2,150	750
	8/10/33	1	25	90	28.7	6.7	7,175	6,030	1,145

TABLE 2.—*Effect of Change in Volume, the Concentration Remaining Constant*

Dog	Time, Hours	Volume In, Cc.	Volume Out, Cc.	Concentration In, Gm. per 100 Cc.	Concentration Out, Gm. per 100 Cc.	Total In, Mg.	Total Out, Mg.	Total Lost, Mg.
179.....	1	25	28	5.3	3.7	1,325	1,036	289
	1	50	51	5.3	4.3	2,650	2,193	457
	1	25	48	10.6	4.5	2,650	2,160	490
	1	50	96	10.9	4.8	5,450	4,608	842
	1	25	71	26.4	7.9	6,600	5,609	991
	1	50	89	26.1	12.3	13,050	10,947	2,103
425.....	1	25	31	5.3	2.9	1,325	899	426
	1	50	46	5.3	4.8	2,650	2,208	442
	1	25	50	10.6	4.6	2,650	2,300	350
	1	50	73	10.9	6.0	5,450	4,380	1,070
	1	25	75	26.4	7.1	6,600	5,325	1,275
	1	50	108	26.3	10.1	13,150	10,908	2,242

more rapidly absorbing membrane, the jejunum, was used. With the change from a 10 to 20 or 25 per cent solution, there was a decided increase in the absorption of dextrose per unit of time (table 1).

Effect of Change in Volume, Concentration Remaining Constant.—With an increase in the volume of fluid introduced into the loop, concentration remaining constant, there was a larger amount of dextrose absorbed. While this difference was most pronounced in the higher (25 per cent) concentrations, it was quite obvious in the lower (from 5 to 10 per cent) concentrations (table 2).

Effect of Increasing Concentration on Fluid Change.—With the lower concentrations of dextrose (1, 2.5 and approximately 5 per cent

solutions), little or no increase in the fluid volume occurred, although secretion occurred in the empty loop. On the contrary, with the lower concentrations, there was an actual loss of fluid through absorption. With the higher concentrations (10 per cent), there was a constant increase in the fluid content of the loop, and with the 25 per cent solution, the increase in fluid volume was proportionately greater. These findings are consistent with those which one would expect when hypotonic and hypertonic solutions are used. Although more dextrose is absorbed from the higher concentrations, fluid is drawn into the colon loop from the patient's body stores.

Effect of a Changing Fluid Volume by Varying Concentration.—There was a rather constant and rapid decrease in the concentration of the dextrose solution within the loop, in a unit of time, when the 5, 10 and 25 per cent solutions were used. This undoubtedly depended on a relatively constant mobilization of fluid and absorption of dextrose. With lower concentrations (from 1 or 2.5 to 5 per cent), the changes in concentration were not so great. Data obtained from dogs in which hypotonic solutions were used indicated that the colon at times was actually capable of withdrawing water from the hypotonic dextrose solutions more rapidly than it took up the dextrose. When rapid fluid absorption is desired, hypotonic solutions are more desirable.

Comparison of Rate of Dextrose Absorption in Chronic Colon Loop of Unanesthetized Animal with Rate of Absorption in Isolated Colon of Intact Anesthetized Animal.—With increasing concentrations of dextrose in the isolated colon of the anesthetized animal, there was an increasing amount of dextrose absorbed. With increasing concentrations in the unanesthetized animals, there was likewise an increase in the fluid volume, as would be expected.

Slightly greater amounts of dextrose were lost for a given concentration in the acute experiments under anesthesia. However, this difference may be explained by the fact that the entire colon was used in the anesthetized dogs and a greater quantity of a given concentration of fluid was employed in each instance. This was shown to result in the absorption of a greater amount of dextrose.

Rate of Absorption in Chronic Colon Loop as Compared with Rate of Absorption in Chronic Jejunal Loop.—The highest average absorption of dextrose from the chronic colon loop (dog 425), when 25 cc. of a 5.8 per cent solution was placed within the loop, was 460 mg. in one hour. The nearest figures of Ravdin and his associates [8] gave an absorption of 260 mg. in one instance when 20 cc. of a 5.3 per cent solution was used, and 607 mg. in another instance when 20 cc of a 5.6 per cent dextrose solution had been placed in the chronic jejunal loop for but fifteen minutes. The highest loss of dextrose from an

approximately 25 per cent solution when 50 cc. had been placed in the colon loop for one hour was 2,790 mg. When 50 cc. of approximately 30 per cent dextrose solution had been placed in the jejunal loop, 2,200 mg. was lost in fifteen minutes. This comparison further substantiates the fact that the colon will absorb dextrose at a much slower rate than the jejunum.

COMMENT

The preparation of a chronic colon loop, as outlined, carried with it a high operative mortality, but once the loop was completed, it offered a means of studying absorption from the colon in the unanesthetized animal whose intestinal loop had its nerve, blood and lymphatic supply intact. This type of chronic loop provides a method for repeated study in the same animal over a long period of time. On the basis of sections removed from one colon loop and from comparison of repeated studies, it appears that these loops remained histologically and physiologically normal over an indefinite period.

It was shown that the rate of absorption of dextrose from the colon increased slightly with increasing concentrations up to 5 per cent, which approximates an isotonic solution. With increasing concentrations beyond this point, there was a decided increase in the rate of dextrose absorbed. It was further shown that with an increase in the volume of solution, concentration remaining constant, there was a decided increase in the dextrose absorbed.

Comparing these data with those obtained on absorption of dextrose from the entire and isolated colon in the anesthetized animal, it is evident that anesthesia per se made but little difference in the conduct of the colon as a physiologic unit. When compared with the results obtained on chronic jejunal loops by Ravdin and his associates,[8] as well as the results obtained in the low ileac loop in the anesthetized animal, it was shown that the colon absorbs dextrose at a much slower rate than does the ileum or jejunum.

These studies substantiate the results of my previous investigation on the absorption of dextrose solution from the colon. It appears that the amount of dextrose absorbed from the colon is too small to be of any considerable clinical value.

CONCLUSIONS

1. The chronic colon loop affords a simple and efficient method for the study of absorption of dextrose solutions from the colon.

2. The rate of absorption of dextrose depends primarily on the concentration of the solution used and the quantity placed within the colon.

3. These studies further substantiate the view that the colon as a means of introduction of dextrose into the body mechanism is inadequate for clinical needs, and, further, actual harm may result from the use of hypertonic solutions, owing to withdrawal of water.

NOTE.—In an article by Cutting just published (Cutting, R. A.: Absorption of Dextrose and Water by the Small Intestine and the Colon, ARCH. SURG. **29**: 643 [Oct.] 1934) exception was taken to my earlier studies because they were conducted "under anesthesia and after extensive intra-abdominal surgical manipulations." The experiments reported in the present paper are devoid of this criticism; yet the conclusions reached are essentially the same as those previously reported. The present data are the only ones reported on experimental animals with a chronic condition.

END-RESULTS OF OPERATION ON THE THYROID GLAND

CARL O. RICE, M.D.
MINNEAPOLIS

Surgical intervention is considered the proper treatment for the various types of thyroid disease; still one must admit that there is much to be desired in this field. It is difficult to evaluate completely the results obtained, even under the best conditions, owing to the numerous variable factors which may be encountered in procuring the data.

Crile [1] reported from the Cleveland Clinic that 86.3 per cent of more than 12,000 patients treated for hyperthyroidism were able to resume their former occupation in less than a year after the operation. Moore [2] reported cures in 82.7 per cent of persons with exophthalmic goiter, in 88.9 per cent of those with adenomatous goiter and in 51 per cent of those with secondary exophthalmic goiter (toxic adenoma). What constitutes a cure he did not state, and therefore it is difficult to know on what basis the cures may be evaluated. From the Portland Clinic, Joyce [3] reviewed the results in 1,066 patients treated by operation, most of whom had exophthalmic goiter or toxic adenoma. Eighty per cent of the patients were well and strong and able to work. His observations were made from three to six years after thyroidectomy. Rapid and irregular heart action was the most common residual symptom. There was recurrence of the goiter in 3.6 per cent of those with adenomatous goiter and in 5.7 per cent of those with hyperplastic goiter. In a small series, Dunhill [4] found that 90 per cent of the patients were able to return to a normal mode of living after thyroidectomy for hyperthyroidism. Coller and Potter,[5] reviewing the cases in University Hospital, Ann Arbor, found that complete rehabilitation occurred in 91.4 per cent of the patients with exophthalmic goiter, in 95.6 per cent of those with toxic adenomas and in 94.5 per cent of those with nontoxic adenoma. How-

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From the Department of Surgery, University of Minnesota.

1. Crile, George: Diagnosis and Treatment of Diseases of the Thyroid Gland, Philadelphia, W. B. Saunders Company, 1932, chap. 39; Thyroidectomy: Its Indications and End-Results, Practitioner **125**:661, 1930.

2. Moore, J. C.: Subtotal Thyroidectomy: Deductions from 1,700 Cases, Northwest Med. **31**:118, 1932.

3. Joyce, Thomas M.: Thyroid Surgery at the Portland Clinic, Ann. Surg. **94**:563, 1931.

4. Dunhill, T. P.: Toxic Goiter, Practitioner **125**:672, 1930.

5. Coller, F. A., and Potter, E. B.: End-Results of Thyroidectomy, Ann. Surg. **94**:568, 1931.

ever, when these apparently satisfactory results were analyzed further, it was found that only 48.3 per cent of the patients with exophthalmic goiter and toxic adenoma had no residual symptoms. Residual cardiac symptoms were found to a greater or less degree in 26.8 per cent of those with exophthalmic goiter and in 34.4 per cent of those with toxic adenomas. It was also pointed out that the patients who were operated on earliest in the course of the disease were more free from residual symptoms after a period of years than those who had the condition for a longer time before surgical intervention was attempted.

Many patients who show only a few residual symptoms and are able to resume their former economic station are, nevertheless, definitely handicapped as a result of the remaining symptoms.

In reviewing Richter's results following thyroidectomy for hyperthyroidism Elliott [6] found that 70 of 100 patients were well, whereas the remaining 30 were aware of some disability. Definite evidence of visceral injury as a result of hyperthyroidism was present in 41. He stated that the failure to obtain ideal results may be attributed largely to the failure to make an early diagnosis, thereby neglecting surgical therapy until damaging and frequently permanent visceral symptoms occur.

Alfred H. Noehren,[7] from the Buffalo clinic for the treatment of thyroid disease, reported the results of 100 consecutive operations three months postoperatively, and concluded that between 80 and 90 per cent of the patients were cured at that time. This period of observation is too short to determine cures, but it is interesting to note that his percentages are comparable to those obtained by other investigators who studied their results over longer periods of time.

MATERIAL FOR THE PRESENT INVESTIGATION

A clinical study of all patients with goiter operated on at the Minnesota General Hospital from January 1918 to January 1931 was undertaken. There were 527 patients. Sixty-nine per cent were female and 31 per cent were male. Patients with toxic goiter constituted approximately 80 per cent. The exact frequency of each type was:

	No. of Cases	Per Cent
Exophthalmic goiter	292	55.6
Toxic adenoma	121	22.8
Nontoxic adenoma	98	18.6
Colloid goiter	7	1.3
Cancer	5	0.9
Thyroiditis	4	0.8

6. Elliott, Charles A.: The Results of Thyroidectomy for Hyperthyroidism from the Internist's Standpoint, Proc. Internat. Assemb. Inter-State Post-Grad. M. A. North America **6**:519, 1930.

7. Noehren, Alfred H.: Results of Thyroidectomy, Ann. Surg. **93**:1045, 1931.

Comments on the symptoms of the various thyroid diseases are so readily available that they have not been included here. It is interesting to note, however, that the average duration of symptoms before operation in the various diseases is somewhat variable, as can be observed in those cases on which sufficient data were obtainable.

Type	No. of Cases	Duration of Hyperthyroidism, Months
Exophthalmic goiter	261	20.1
Toxic adenoma	112	34.4

Type	No. of Cases	Duration of Goiter, Months
Nontoxic adenoma	82	66.5
Colloid goiter	5	109.4
Cancer	5	51.2

The average duration of the cases of exophthalmic goiter in which complete cures were reported was less than that of those in which cures were not satisfactory. This did not appear to be true of the cases of toxic adenoma, but the discrepancy may have been due to the fact that there were not enough cases in this group to make conclusions from them reliable. Percentage of improvement in relation to the duration of symptoms was as follows:

	No. of Cases	Duration of Symptoms, Months
Exophthalmic goiter		
100% improved	28	10.9
75 to 99% improved	69	18.0
0 to 74% improved	15	53.0
Toxic adenoma		
100% improved	9	29.3
75 to 99% improved	25	24.3
0 to 74% improved	7	22.8

The response of the pulse rate and basal metabolic rate to the administration of iodine preoperatively was interesting. In the patients with exophthalmic goiter the pulse rate and basal metabolic rate showed a definite decline except in a few instances. In the group with toxic adenoma, this reaction was not as uniform. Some patients showed a definite decline in the pulse rate, but others showed an increase or no change. These facts are being investigated from a statistical standpoint, and will be dealt with in a subsequent article.

END-RESULTS

In an effort to determine the end-results obtained, follow-up letters were sent to all patients, and subsequent examinations were made whenever possible. Many could not be traced, owing to change of address or to lack of response to the letters. Two hundred and ten

replies were received. Only a few patients (27) returned for personal observation. The results observed in that group corresponded well with those reported in response to the questionnaire, but in view of the fact that there was not a sufficient number of cases from which to draw accurate conclusions, they were left out of consideration in the tabulations, in order to avoid the possibility of confusing the end-results.

An effort was made to estimate the percentage of improvement in each case on the basis of information received in answer to the questionnaire. The patients who reported no residual symptoms were graded 100 per cent improved. The others were graded by estimating from the response to the questionnaire, much as one would study an examination paper, the percentage of improvement in each case. These estimations are, of course, not free from error, and are subject to the same criticism that one may attach to the results from any questionnaire. Figures were used in an attempt to establish something more tangible than is expressed by the words excellent, good, fair, poor and rehabilitated, which are fraught with as much possibility for variation as would be expected from the numerical estimations.

The questionnaires were examined by Dr. Adam Smith (internist), and it was found that his grading corresponded, on the whole, very closely with mine. He estimated the same number of patients as cured, but graded each of the improved patients as having approximately 5 per cent more disability. This seems to indicate that the questionnaires have been properly evaluated, for in all probability the estimations of two men could not approach one another more closely. The degree of improvement was as follows:

	No. of Cases	Per Cent	
Exophthalmic goiter	125		
Perfect (100% improved)	30	24.0	81.6% satisfactorily rehabilitated
Excellent (85 to 99% improved)	60	48.0	
Good (75 to 84% improved)	12	9.6	
Fair (50 to 74% improved)	5	4.0	
Poor (1 to 49% improved)	3	2.4	
No improvement	12	9.6	
Dead subsequently	3	2.4	
Toxic adenoma	51		
Perfect	10	19.6	76.4%
Excellent	23	45.1	
Good	6	11.7	
Fair	0	0.0	
Poor	3	5.8	
No improvement	4	7.8	
Dead subsequently	5	9.8	
Nontoxic adenoma	23		
Perfect	5	21.7	73.7% satisfactorily rehabilitated
Excellent	8	34.7	
Good	4	17.3	
Fair	1	4.3	
Poor	0	0.0	
No improvement	4	17.3	
Dead subsequently	1	4.3	

It is evident from the preceding record that although only a small percentage of the patients obtained perfect results, a large group obtained satisfactory results and could be classified as cured, rehabilitated or able to resume their former economic station. In the patients graded from 75 to 90 per cent improved many of the residual symptoms were of minor importance and did not appreciably incapacitate the patient. Cardiac palpitation, dyspnea on exertion, weakness of the legs and tremor of the hands were the residual symptoms most frequently observed. They were minimal in many cases.

Eighty-seven per cent of those who responded to the questionnaire said they were better after the operation than before. On closer inspection of the individual questions it was discovered that some persons were only slightly better. Some of the questions were completely ignored. A tabulation of the answers revealed the following results:

Do you feel better, worse or the same as before your operation?

Better	184	87.6%
Worse	8	3.8%
The same	16	7.6%
No reply	2	0.9%

Is your nervousness more, less or the same as before your operation?

More	191	4.2%
Less	161	76.6%
The same	33	15.7%
No reply	7	3.3%

Does your heart pound or flutter?

Yes	79	37.1%
No	102	48.5%
No reply	29	13.8%

Have you gained or lost weight or is it the same as before your operation?

Gained	169	80.4%
Lost	13	6.1%
The same	9	4.2%
No reply	19	9.4%

Do you perspire too easily?

Yes	57	27.1%
No	105	50.0%
No reply	48	22.8%

Is your appetite good, poor or too good?

Good	127	60.4%
Poor	12	5.7%
Too good	22	10.4%
No reply	49	23.3%

Do you become short of breath when walking upstairs?

Yes	88	41.9%
No	83	39.5%
No reply	37	17.6%

Do you have any shaking of your hands?

Yes	46	21.9%
No	119	56.6%
No reply	45	21.4%

Do you have any diarrhea?

Yes	16	7.6%
No	184	87.6%
No reply	10	4.7%

Has your goiter grown since your operation?

Yes	17	8.0%
No	157	74.7%
No reply	36	17.1%

Do you notice any weakness in your legs now?

Yes	70	33.3%
No	119	56.6%
No reply	21	10.0%

Are you stronger, weaker or the same as before your operation?

Stronger	135	64.2%
Weaker	27	12.8%
The same	32	15.2%
No response	16	7.6%

Is the scar on your neck rough or smooth?

Rough	19	9.0%
Smooth	142	67.6%
No reply	49	23.3%

Have you noticed any change in your voice since the operation?

Yes	32	15.2%
No	63	30.0%
No reply	115	54.7%

Are your eyes more prominent, less prominent or the same as before your operation?

More	13	6.1%
Less	28	13.3%
The same	39	18.5%
No reply	130	61.8%

Have you any other ailments? If so, what?

Yes	92	43.8%
No	65	43.8%
No reply	53	25.2%

By further investigation of the response to the last question it was shown that of the patients whose improvement was less than 75 per cent, 70.7 per cent had other ailments, whereas of those whose improvement was graded 75 per cent or more, only 38.2 per cent had other ailments. This may be significant only to the extent that it suggests that some of the symptoms which had been attributed to goiter, perhaps by both the physician and patient, may have had their origin elsewhere.

The other ailments were variable, and included gynecological disorders, disease of the gallbladder, "dyspeptic" troubles, intestinal disorders, frequent headaches, dizzy spells and fainting spells. Anything which could not be attributed definitely to the thyroid condition was included among the other ailments. A check on the other ailments has not been included in this study.

The hospital mortality for the entire group was 2.2 per cent. This is a little higher than was found in a more recent series, which showed

1.36 per cent during the years from 1928 to 1931.[8] The difference may be accounted for, however, by the fact that the entire group includes patients operated on before the use of iodine had become established and also includes patients operated on by seventeen surgeons over a period of twelve years. Crile reported an operative mortality of 0.86 per cent. Goetsch[9] had an operative mortality of 1.25 per cent in a series of 1,755 cases. He remarked that the fatal outcome was not related to the type of operation, for it occurred after ligation, lobectomy or bilateral subtotal thyroidectomy. It was his opinion that the injudicious use of iodine was a contributing factor in increasing the risk, by making the patient refractory to iodine.

An estimation of the results based on the amount of thyroid tissue remaining was not made, because there were so many surgeons involved and the possibility of error in matching one surgeon's "third of a normal-sized lobe" with that of another would be too great. Until the amount can be more accurately expressed such an estimation will be without value.

CONCLUSIONS AND SUMMARY

It appears that the results from operation on the thyroid are by no means ideal. It seems safe to state that approximately 25 per cent of the patients will receive perfect results, 60 per cent more will obtain satisfactory results, and the remaining 15 or 20 per cent will remain more or less incapacitated and may even require further therapy.

Eighty-seven per cent of those who responded to the questionnaire indicated that they were improved. The subsequent course of those with poor results has not been accurately ascertained. Some have returned for a second operation and others have received roentgen-ray therapy, but most of them have not been followed up, owing to the lack of adequate follow-up methods at the time of operation.

The shorter the duration of hyperthyroidism the more satisfactory were the results following thyroidectomy.

The administration of iodine caused a definite improvement, with a reduction in the pulse rate and basal metabolic rate, in patients with exophthalmic goiter. Patients with toxic adenoma failed to show uniformly an improvement after the administration of iodine.

Only a few patients (11 per cent) reported no improvement.

More accurate diagnosis and evaluation of the other symptoms might aid in the elimination of surgical treatment for those patients who suffer from ailments not related to thyroid disease which may be the underlying factor in their disability.

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8. Rice, Carl O.: Comparison of the Goiters from the State of Minnesota with Those from the Canton of Bern, Switzerland, West. J. Surg. **40**:506, 1932.

9. Goetsch, Emil: Mortality in Goiter Operations, Ann. Surg. **94**:167, 1931.

The results obtained in this clinic from roentgen-ray treatment of exophthalmic goiter are being investigated by Dr. Adam Smith. Anticipating these results after observing many of the cases, it appears that with the exception of the time factor the end-results from surgical or roentgen-ray therapy will be found to approach each other closely. However, the time factor may be the most important feature in the cure of exophthalmic goiter as indicated in this article, because during the six to nine months which are required to obtain results by roentgen-ray therapy the patient may become definitely more toxic. Therefore the choice of surgical intervention in preference to roentgen-ray therapy may be an important factor in determining the end-result to the best advantage of the patient.

1218 Medical Arts Building

INFLUENCE OF EXPOSURE TO COLD AND OF DEPRIVATION OF FOOD AND WATER ON THE DEVELOPMENT OF SHOCK

ALFRED BLALOCK, M.D.
NASHVILLE, TENN.

My earlier experiments [1] and those of Parsons and Phemister [2] showed that severe trauma to an extremity causes a sufficient loss of red blood cells and of blood plasma into the injured tissues to account for the associated decline in blood pressure. These studies were performed at room temperature on animals which had not been deprived of food and water. The present experiments were carried out to determine the effects of cold and of the deprivation of food and water on the minimum loss of blood necessary to produce death. Loss of blood was produced in some instances by the removal of blood through a cannula that had been placed in the femoral artery and in others by injury to the muscles.

METHODS

All of the animals were anesthetized and exhibited no evidence of pain. A cannula that was connected to a mercury manometer was introduced into the femoral or carotid arteries in order that the blood pressure might be determined. In the experiments in which the effects of bleeding were studied, whole blood equaling 1 per cent of the body weight was removed from the femoral artery at one hour intervals until death occurred. In the experiments in which the effects of injury to the muscles were studied, the trauma was produced by striking one of the posterior extremities repeated blows with a hammer. Following death in the latter experiments, the difference in the weights of the traumatized and non-traumatized posterior extremities was determined by a method that has been described previously.[1] Hematocrit determinations were performed in some of the studies.

In some of the experiments in which the influence of exposure to cold was studied, pentobarbital sodium was used as the anesthetic. The pentobarbital sodium was introduced intravenously in the dosage of 30 mg. per kilogram of body weight. If normal animals are given this amount of pentobarbital sodium, they usually regain consciousness in approximately four hours. In several instances it was necessary to supplement the initial injection by additional pentobarbital sodium in

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From the Department of Surgery of Vanderbilt University.

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1. Blalock, Alfred: Experimental Shock: The Cause of the Low Blood Pressure Produced by Muscle Injury, Arch. Surg. **20**:959 (June) 1930.

2. Parsons, E., and Phemister, D. B.: Hemorrhage and Shock in Traumatized Limbs, Surg., Gynec. & Obst. **51**:196, 1930.

order to maintain deep anesthesia. In other experiments, large doses of morphine were used as the anesthetic. In the studies in which an extremity was traumatized, the morphine was supplemented by ether anesthesia while the trauma was being produced. In a few experiments, sodium barbital (0.3 Gm. per kilogram of body weight administered intravenously) was used as the anesthetic. The temperature of the room was approximately 4 C. (39.2 F.). The rectal temperature of the animals was determined frequently.

In the experiments in which the influence of deprivation of food and water was studied, sodium barbital (0.3 Gm. per kilogram of body weight administered intravenously) was used as the anesthetic. No food or water was given during the forty-eight hours preceding the injection of the barbital. One hour following the introduction of the barbital, blood was removed from the femoral artery, or an extremity was traumatized.

EXPERIMENTAL RESULTS

Exposure to Cold.—Pentobarbital Sodium as the Anesthetic: Twenty control experiments were performed in which the effects of exposure to cold under pentobarbital sodium anesthesia were studied. No bleeding was produced. In ten of the experiments, additional pentobarbital sodium was administered during the course of the observations. All of the animals with the exception of four died. The length of time that the remaining sixteen lived varied from one hour and forty-five minutes to fifteen hours. The average period of survival was five hours and forty-six minutes. The terminal decline in the arterial blood pressure in all the experiments was abrupt. The blood pressure usually remained at a high level until a short time before death. Associated with a marked slowing of the respiratory rate, a rise in blood pressure occurred, and this was followed in a short while by a decline of the blood pressure to zero. In several experiments the respiratory movements ceased about ten minutes before the heart stopped beating. The rectal temperature at the time of death in the various experiments varied from 21.5 to 32.8 C. (70.7 to 91 F.). The average terminal temperature in the sixteen experiments in which death occurred was 25.85 C. (78.53 F.). There was an increase in the concentration of the red blood cells in all of the experiments in which hematocrit determinations were performed. In one experiment the percentage of red blood cells increased from 40 at the time of the control studies to 56 at the time of death, an increase of 40 per cent of the original hematocrit determination. In another the increase was from 49.6 to 66.6 per cent. The smallest increase that was observed in an experiment in which death resulted was from 40 to 43.6 per cent. The results of these experiments are given in table 1.

Nineteen experiments were performed in which blood was removed from the femoral artery of animals which had been given pentobarbital sodium and exposed to cold surroundings. Additional pentobarbital

TABLE 1.—*The Effects of (1) Exposure to Cold, (2) Exposure to Cold and Hemorrhage and (3) Exposure to Cold and Trauma (Pentobarbital Sodium Anesthesia)*

Cold Control					Cold and Hemorrhage						Cold and Trauma					
Experiment	Time Lived	Terminal Temperature	Character of Decline in Blood Pressure	Change in Hematocrit, per Cent*	Experiment	Time Lived	Terminal Temperature	Amount Bled, per Cent of Body Weight	Character of Decline in Blood Pressure	Change in Hematocrit, per Cent*	Experiment	Time Lived	Terminal Temperature	Difference in Weight of Extremities, per Cent of Body Weight	Character of Decline in Blood Pressure	Change in Hematocrit, per Cent*
1	5 hrs. 35 min.	28.8	Abrupt		1	5 hrs. 35 min.	26.6	5.0	Gradual		1	3 hrs. 20 min.	23.0	1.0	Abrupt	
2	3 hrs. 10 min.	25.4	Abrupt		2	5 hrs.	?	5.0	Gradual		2	3 hrs. 20 min.	24.2	1.5	Abrupt	
3	5 hrs. 10 min.	32.8	Abrupt		3	6 hrs. 10 min.	?	5.8	Gradual		3	52 hrs.	17.8	6.1	?	
4	15 hrs.	?	?		4	5 hrs. 35 min.	?	5.5	Gradual		4	4 hrs. 55 min.	20.9	5.2	Gradual	
5	4 hrs. 10 min.	24.3	Abrupt		5	6 hrs.	28.3	5.5	Gradual		5	3 hrs. 45 min.	25.6	1.8	Abrupt	
6	8 hrs.	?	Abrupt		6	5 hrs. 45 min.	29.4	5.5	Gradual		6	2 hrs. 50 min.	30.2	2.0	Abrupt	
7	2 hrs. 25 min.	26.0	Abrupt		7	7 hrs. 20 min.	35.1	7.0	Gradual		7	6 hrs. 15 min.	28.0	5.0	Fairly gradual	
8	3 hrs. 40 min.	23.6	Abrupt		8	2 hrs. 30 min.	28.2	2.0	Abrupt		8	(8 hrs.) Killed	(37.0)	(4.7)	Still up	
9	3 hrs. 10 min.	29.3	Abrupt		9	6 hrs. 35 min.	28.9	6.0	Gradual		9	(24 hrs.) Killed	(36.8)	(4.4)	Still up	(+ 2.0)
10	5 hrs.	22.9	Moderately abrupt		10	6 hrs.	28.1	5.3	Gradual		10	8 hrs. 13 min.	20.0	4.7	Gradual	— 8.0
11	1 hr. 45 min.	30.7	Abrupt	+25	11	6 hrs. 55 min.	27.2	6.0	Gradual		11	4 hrs. 55 min.	27.7	3.6	Abrupt	+21.0
12	2 hrs. 35 min.	24.6	Abrupt	+24	12	1 hr. 30 min.	30.0	1.0	Abrupt		12	1 hr. 50 min.	28.7	2.0	Abrupt	+30.0
13	(8 hrs.) Recovery	(29.8)	Still up	(+21)	13	5 hrs. 25 min.	29.0	5.0	Gradual		13	2 hrs. 15 min.	30.0	2.8	Abrupt	+16.0
14	4 hrs. 50 min.	21.5	Abrupt	+40	14	4 hrs. 30 min.	25.5	4.0	Gradual	+11	14	7 hrs. 45 min.	30.0	4.0	Fairly gradual	0
15	4 hrs.	22.2	Abrupt	+34	15	6 hrs. 40 min.	32.8	6.5	Gradual	0						
16	9 hrs. 15 min.	?	Abrupt	?	16	5 hrs. 30 min.	24.5	5.3	Gradual	— 3	Aver.	8 hrs. 27 min.†	25.52	3.31		
17	(8 hrs.) Recovery	(42.0)	Still up	(+ 6)	17	3 hrs. 35 min.	25.3	3.5	Gradual	— 3						
18	6 hrs. 50 min.	24.0	Abrupt	+ 9	18	3 hrs. 45 min.	27.2	3.0	Abrupt	+ 2						
19	(8 hrs.) Recovery	(40.2)	Still up	(+ 3)	19	5 hrs. 40 min.	34.8	5.5	Gradual	—21						
20	(8 hrs.) Recovery	(35.8)	Still up	(+16)	Aver.	5 hrs. 16 min.	28.87	4.86								
Aver.	5 hrs. 46 min.	25.85														

* The hematocrit value was calculated by determining the difference in the hematocrit readings during the control period and that at the time of death and dividing this difference by the reading for the control period.

† This includes the experiment in which the duration was fifty-two hours.

sodium was given to six of the animals. As has been stated, whole blood equaling 1 per cent of the body weight was removed each hour until death occurred. The duration of the experiments varied from one hour and thirty minutes to seven hours and twenty minutes. The average duration of the experiments was five hours and sixteen minutes. The decline in the blood pressure was gradual in sixteen of the nineteen experiments. In the remaining three, the blood pressure remained at a high level until shortly before death, when an abrupt decline took place. The loss of blood that was associated with death in these three experiments was small. In one experiment it equaled 2 per cent of the body weight; in the second, 1 per cent, and in the third, 3 per cent. The total quantity of blood that was removed in the various experiments varied from 1 to 7 per cent of the body weight. The average amount removed in the nineteen experiments equaled 4.86 per cent of the body weight or approximately one half of the estimated blood volume. The rectal temperature of the animals at the time of death varied from 24.5 to 35.1 C. (76.1 to 95.2 F.). The animal which tolerated hemorrhage best had the highest temperature at the time of death. Hematocrit determinations were performed frequently in six of the experiments. In all instances, an increase in the concentration of the red blood cells was noted during the early part of the experiments. When the blood pressure fell to a low level, dilution of the red cells occurred. At the time of death, the hematocrit reading was approximately the same as it had been during the control period in four of the experiments. In one experiment a slight concentration persisted, and in the remaining experiments there was a definite dilution. The animal in which the marked terminal dilution of the red blood cells occurred had the highest temperature at the time of death. The figures in the table that refer to hematocrit readings are concerned only with a comparison of the determinations during the control period and those at the time of death. The results of these experiments are given in table 1.

Fourteen experiments were performed in which one of the posterior extremities of animals anesthetized by pentobarbital sodium and exposed to cold surroundings was traumatized. Additional pentobarbital sodium was subsequently injected in five of the experiments. Two animals in which the temperatures were essentially normal and in which the mean arterial pressures were greater than 100 mm. of mercury were killed eight and twenty-four hours, respectively, after the beginning of the experiments. The difference in the weights of the posterior extremities was 4.7 per cent of the body weight in one of the experiments and 4.4 per cent in the other. The results of these experiments are not included in the average in the tables. The duration of the remaining twelve experiments varied from one hour and fifty minutes to fifty-

two hours. The average duration was eight hours and twenty-seven minutes. Excluding the experiment in which the animal lived for fifty-two hours, the average duration was four hours and twenty-nine minutes. In seven of the experiments, death was preceded by a slowing of the respiratory movements and an abrupt decline in the arterial pressure from a fairly high level to zero. It was in these experiments that the difference in the weights of the traumatized and nontraumatized extremities was least. The difference in the weights of the traumatized and nontraumatized extremities varied from 1 to 6.1 per cent of the body weight. The average difference equaled 3.31 per cent. The temperature at the time of death in the different experiments varied from 20 to 30.2 C. (68 to 86.3 F.). The average rectal temperature at the time of death was 25.52 C. (77.93 F.). Following the traumatization, there was an increase in the concentration of the red blood cells in the five experiments in which hematocrit determinations were performed. A dilution of the red blood cells occurred shortly before death in two of the experiments, and the hematocrit readings were approximately the same at the time of death in these two experiments as they had been during the control period. That a marked increase in the concentration of the blood is not a necessary feature of the fatal results in these animals was shown in one experiment in which the hematocrit reading reached during the control period was 28.7 and the highest reading reached during the experiment was 33.9. In another experiment the maximum alteration in the hematocrit readings was from 33.8 to 38.8. The greatest alteration in the hematocrit readings that was observed was from 39.4 during the control period to 47.5 at the time of death. The figures in the tables that have to do with hematocrit readings refer only to a comparison of those obtained during the control period and at the time of death. The results of these experiments are given in table 1.

Sodium Barbital as the Anesthetic: Experiments in which sodium barbital was used as the anesthetic instead of pentobarbital sodium were also performed, and the effects of exposure to cold, of cold and hemorrhage and of cold and trauma were studied. The results were similar to those obtained when pentobarbital sodium was used as the anesthetic. They differed in that the period of survival of the animals was somewhat shorter and in that the amount of hemorrhage tolerated was slightly less.

Morphine as the Anesthetic (Supplemented by Ether in Cases of Trauma): The effects of exposure to cold were studied in four experiments in which morphine was used as the anesthetic. Death occurred nine hours following the beginning of one of the experiments. The respiratory rate a short time before death was 3 per minute. The terminal temperature was 16.8 C. (62.2 F.). The duration of another of

TABLE 2.—*The Effects of (1) Exposure to Cold and Hemorrhage and (2) Exposure to Cold and Trauma (Morphine Anesthesia Supplemented by Ether During Traumatization)*

Cold and Hemorrhage						Cold and Trauma					
Experiment	Time Lived	Terminal Temperature	Change in Hematocrit, per Cent*	Amount Bled, per Cent of Body Weight	Character of Decline in Blood Pressure	Experiment	Time Lived	Terminal Temperature	Change in Hematocrit, per Cent*	Difference in Weight of Extremities, per Cent of Body Weight	Character of Decline in Blood Pressure
1	6 hrs. 5 min.	22.6	—36.5	6.0	Gradual	1	6 hrs. 30 min.	18.6	+ 2.1	3.18	Gradual
2	6 hrs. 30 min.	23.0	—35.2	6.5	Gradual	2	7 hrs. 20 min.	20.2	+16.2	3.41	Gradual
3	6 hrs. 30 min.	27.6	—42.3	6.5	Gradual	3	10 hrs.	20.0	.....	5.24	Gradual
4	6 hrs. 40 min.	28.9	—22.3	6.5	Gradual	4	6 hrs. 40 min.	23.6	—15.9	5.86	Gradual
5	6 hrs. 30 min.	26.5	—17.8	6.4	Gradual	5	7 hrs. 30 min.	16.0	—23.1	5.22	Gradual
Average	6 hrs. 27 min.	25.7	—30.8	6.38	Gradual	Average	7 hrs. 36 min.	19.7	.....	4.56	Gradual

* The hematocrit value was calculated by determining the difference in the hematocrit readings during the control period and at the time of death and dividing this difference by the reading for the control period.

the experiments was fifteen hours. The terminal temperature was not determined. Observations were discontinued in the remaining two experiments after twenty-three hours. The rectal temperatures at the end of this time were essentially normal. These experiments indicate that exposure to cold is tolerated better by animals narcotized by morphine than by those anesthetized by pentobarbital sodium or barbital.

Five experiments were performed in which hemorrhage and exposure to cold were studied in animals anesthetized by morphine. The average duration of the experiments was six hours and twenty-seven minutes; the average rectal temperature at the time of death was 25.7 C. (78.2 F.), and the average amount of blood removed in terms of body weight

TABLE 3.—*Studies on (1) Bleeding and (2) Trauma in Animals Deprived of Food and Water for Forty-Eight Hours*

Bleeding			Trauma		
Experiment	Duration	Amount Bled, per Cent of Body Weight	Experiment	Duration	Difference in the Weight of the Posterior Extremities, per Cent of Body Weight
1	3 hrs. 5 min.	4.00	1	5 hrs. 12 min.	4.47
2	4 hrs. 22 min.	5.00	2	8 hrs. 19 min.	4.64
3	4 hrs. 10 min.	5.00	3	7 hrs. 50 min.	5.77
4	2 hrs. 10 min.	3.00	4	6 hrs. 4 min.	4.80
5	4 hrs. 45 min.	5.50	5	6 hrs.	4.87
6	5 hrs.	6.00	6	5 hrs. 55 min.	3.32
7	3 hrs. 55 min.	4.50	7	3 hrs. 10 min.	3.28
8	4 hrs. 50 min.	5.50	8	4 hrs. 20 min.	4.43
9	2 hrs.	2.75			
Average	3 hrs. 40 min.	4.58	Average	5 hrs. 51 min.	4.45

was 6.38 per cent. The concentration of the red blood cells increased during the early part of four of the five experiments, but a marked terminal dilution occurred in all instances. The decline in the blood pressure in all of the experiments was gradual. The results of these experiments are given in table 2.

Five experiments were performed in which trauma and exposure to cold were studied in animals anesthetized by morphine alone except for the addition of an inhalation ether anesthetic during the time in which the trauma was being produced. The average duration of the experiments was seven hours and thirty-six minutes; the average rectal temperature at the time of death was 19.7 C. (67.5 F.), and the average difference in the weights of the traumatized and nontraumatized extremities as expressed in terms of body weight was 4.58 per cent. A dilution of the red blood cells occurred in some experiments, and a concentration in others. The decline in the blood pressure in all of the experiments was gradual. The results of these experiments are to be found in table 2.

Deprivation of Food and Water.—As has been stated, the animals were deprived of food and water for forty-eight hours preceding the experiments, and sodium barbital was used as the anesthetic. Nine experiments were performed in which at one hour intervals blood equaling 1 per cent of the body weight was removed from the femoral artery. This was continued until death occurred. The average duration of these experiments was three hours and forty-nine minutes. The average amount of blood removed in the nine experiments equaled 4.58 per cent of the body weight. The results of the experiments are enumerated in table 3.

In eight experiments, one of the posterior extremities was traumatized. The average length of time that the animals lived following the traumatization was five hours and fifty-one minutes. The average difference in the weights of the traumatized and nontraumatized extremities was 4.45 per cent of the body weight. The results of these experiments are to be seen in table 3.

COMMENT

Influence of Exposure to Cold.—Concerning the relationship of the external temperature to shock, Cannon [3] stated:

> That the incidence and severity of shock are in some way related to the coldness of the surroundings of the wounded man seems well established. Members of shock teams working in the A.E.F. during the summer and fall of 1918 reported the strikingly larger number and the greater severity of the cases of shock in the cold, wet months of the fall, September and October, as contrasted with the cases seen during the fighting in the warm weather of July and August.

Observations such as these prompted Bayliss and Cannon [4] to perform experiments on the effects of low temperatures. It was found that the blood pressure of an animal anesthetized by ethyl carbamate (urethane) could be greatly reduced by cold surroundings. They stated:

> This effect, however, was chiefly due to slowing of the heart beat, the pressure falling with the rate. When the animal was warmed, there might be complete recovery of the normal pressure. On the other hand, probably some additional effect is produced besides that on the heart, for, after slight hemorrhage, cooling resulted in a fall of pressure which was not restored when the animal was warmed.

It has been shown [5] that dogs and cats may recover after the body temperature has reached 19 C. (66.2 F.). An instance of complete recovery in a person whose temperature had fallen on exposure to 24 C. (75.2 F.) is recorded.[5]

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3. Cannon, W. B.: Traumatic Shock, New York, D. Appleton & Company, 1923, p. 90.

4. Cannon,[3] p. 93.

5. Britton, S. W.: Extreme Hypothermia in Various Animals and in Man, Canad. M. A. J. **22**:257, 1930.

The present experiments were performed primarily in order to obtain a comparison of the effects of hemorrhage outside the body, as from the exposed femoral artery, and of hemorrhage into the injured tissues of an extremity when the animals were exposed to a low temperature. The short period of survival of the animals which were simply given pentobarbital sodium and exposed to cold was surprising. The average rectal temperature at the time of death was 25.85 C. (78.53 F.). This is approximately what one would anticipate in view of previous work. In this connection, Barbour [6] stated: ". . . chemical regulation must break down rapidly, for Storm van Leeuwen has shown that cooling tends to reduce the reflex irritability of the spinal cord. This reduction becomes very marked at a body temperature of 26°, which may explain why this temperature approximates the lowest compatible with life." In two of the control experiments, the rectal temperature was more than 30 C. (86 F.) at the time of death, and it is not known why the subjects succumbed. The alterations in the blood pressure in these experiments were somewhat different from those found by Bayliss and Cannon.[4] There was a slow, gradual decline in the pressure in their experiments. In the present experiments, the arterial pressure usually remained at essentially the normal level until shortly before death, when it rose slightly and then fell abruptly. This was associated with a slowing of the heart rate, but death seemed to be due to respiratory failure, as the respirations ceased before the heart stopped beating. It is well known that exposure to cold is associated with an increase in the concentration of the red blood cells. This finding was confirmed in the present experiments, in most of which the increase in the concentration was marked. The slowing of the circulatory flow that is associated with a large increase in concentration of the blood is probably partially responsible for the fatal outcome in these experiments. That it could not be wholly responsible is demonstrated in one experiment in which the hematocrit readings were 40 during the control period and 43.6 at the time of death. The circulatory flow is also slowed by an increase in the viscosity of the blood. Denning and Watson [7] found that the viscosity is increased 3 per cent with a fall of 1 degree C. (1.8 degree F.) and that the temperature factor is more effective the larger the number of corpuscles present.

In the experiments in which blood was removed from the femoral artery of animals anesthetized by pentobarbital sodium, the average temperature at the time of death was 3 degrees higher than that of the

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6. Barbour, H. G.: The Heat-Regulating Mechanism of the Body, Physiol. Rev. **1**:299, 1921.

7. Denning and Watson: The Viscosity of the Blood, Proc. Roy. Soc., London, s.B **78**:353, 1906.

control studies, despite the fact that there was a difference of only thirty minutes in the average duration of the two groups of experiments. The amount of blood removed was less than 5 per cent of the body weight or approximately one half of the total blood volume in only five of the nineteen experiments in which death was produced by bleeding. In three of these experiments, death was associated with an abrupt decline in the blood pressure from a high level to zero, just as was found in most of the control studies. When animals which are not exposed to cold are bled each hour an amount equaling 1 per cent of the body weight, death usually occurs after the fifth or sixth bleeding or after a little more than half of the estimated blood volume has been removed. Hence, it is to be noted in experiments of the duration reported here that exposure to cold does not usually lessen greatly the tolerance to hemorrhage. Had smaller amounts of blood been removed at hourly intervals, it is likely that the total hemorrhage withstood would have been less. This, however, did not seem to be a desirable or necessary experimental procedure, since the duration of life in the studies in which whole blood was removed was approximately the same as that in the experiments in which the animals were simply given pentobarbital sodium and exposed to cold. Hemorrhage and exposure to cold were associated with an increase in the concentration of the red blood cells which became less marked or was replaced by a dilution when the blood pressure fell to a low level. The increase in the concentration was not nearly so marked as that observed in the control experiments. In brief, the control experiments on exposure to cold under pentobarbital sodium anesthesia and those in which blood was removed under similar conditions were of approximately the same duration; a more marked increase in the concentration of the red blood cells was found usually in the control experiments, and the decline in the arterial blood pressure in the experiments on hemorrhage was usually gradual, while in the control studies there was an abrupt terminal decline in the pressure.

There was a great variation in the results of the experiments in which trauma was produced under pentobarbital sodium anesthesia. One of the animals lived fifty-two hours; the difference in the weights of the traumatized and nontraumatized extremities equaled 6.1 per cent of the body weight, and the temperature at the time of death was 17.8 C. (64 F.). As an example of the other extreme, one animal lived one hour and fifty minutes, the difference in the weights of the two posterior extremities was 2 per cent of the body weight, and the terminal temperature was 28.7 C. (83.7 F.). Two of the animals in which traumatization was produced were killed eight and twenty-four hours, respectively, following the beginning of the experiments. It is interesting that the arterial blood pressure had not declined much in these

experiments, that the temperature was essentially normal, and that the difference in the weights of the extremities indicated a loss of almost half of the blood volume into the injured area. The survival period of the traumatized animals corresponded more closely to that found in the control experiments than to that encountered in the experiments in which whole blood was removed. That is to say, the shortest and the longest survival periods were found in the control experiments and in the experiments in which trauma was produced. The average rectal temperature at the time of death of the traumatized animals was slightly lower than that found in the control experiments and more than 3 degrees lower than that found in the studies on hemorrhage. In six of the experiments the difference in the weights of the traumatized and nontraumatized extremities amounted to at least 4 per cent of the body weight. These figures correspond closely to those that were found [1] when traumatization was performed without exposure of the animal to cold. However, in the remaining experiments, the loss of fluid into the injured area was not by itself sufficient to cause death. The decline in blood pressure was gradual in the experiments in which the loss of fluid was great enough to account for death, whereas there was an abrupt terminal decline in the pressure in the experiments in which the loss of fluid was smaller. The behavior of the blood pressure in the latter experiments was similar to that encountered in the control studies of pentobarbital sodium anesthesia. The amount of fluid that was lost into the injured area did not bear any constant relationship to the temperature at the time of death. That an increase in the concentration of the red blood cells was not the main factor in causing death in the experiments in which the local loss of fluid was small was shown in two experiments in which no marked concentration occurred. One is then faced with the question as to what caused the death of the animals in which the part of the circulating blood volume that escaped into the injured area was not great. A comparison of the results of these experiments with those obtained in other experiments in which morphine was used as the anesthetic indicates that the pentobarbital sodium anesthesia in the presence of cold was the main cause.

In the dosages that were used in the present experiments, the anesthesia that is produced by sodium barbital is more profound and of longer duration than that produced by pentobarbital sodium. It is likely for this reason that the animals anesthetized by barbital and exposed to cold survived for a shorter period of time and withstood hemorrhage less well than those in which pentobarbital sodium was used.

That exposure to cold may cause the death of animals anesthetized by morphine was demonstrated by the fatal outcome in less than sixteen hours in two of the four experiments. However, in studies of the

duration of those experiments in which the effects of hemorrhage and of trauma were noted, exposure to cold did not greatly alter the results. These experiments were of approximately seven hours' duration. The decline of the blood pressure in these experiments was gradual, while in many of the experiments in which pentobarbital sodium or barbital was used it was abrupt. The average loss of blood resulting in death in the experiments in which blood was removed was 6.38 per cent of the body weight or more than half of the total blood volume. A greater loss than this is not tolerated by animals which are not exposed to cold. The average difference in the weights of the traumatized and nontraumatized extremities in the five experiments in which injury was produced was 4.58 per cent of the body weight. It is to be noted that this figure is definitely less than that obtained in the experiments on hemorrhage. This difference may be due to the fact that ether as well as morphine was used in the experiments in which trauma was instituted. The more rapid decline in the temperature in the experiments on trauma may have exerted some effect. The average terminal temperature in the experiments on hemorrhage was 25.7 C. (78.3 F.), while that in the studies on trauma was 19.7 C. (67.5 F.).

Influence of Deprivation of Food and Water.—A comparison of the results found in the present experiments with those obtained previously in experiments [8] in which food and water were allowed indicates that depriving animals of food and water for forty-eight hours does not lessen greatly the loss of fluid from the blood stream that is associated with death. This applies both to the experiments in which whole blood was removed from the femoral artery and to those in which one of the posterior extremities was traumatized. The average quantity of blood removed from the femoral artery resulting in death was approximately the same as the average difference in the weights of the traumatized and nontraumatized extremities in the experiments in which injury was produced.

SUMMARY

Animals anesthetized by pentobarbital sodium were exposed to a temperature of approximately 4 C. (39.2 F.). The blood pressure and rectal temperature were determined frequently, and in some instances hematocrit readings were performed. Death occurred in most of the experiments. The average survival period was approximately six hours. The average terminal rectal temperature was 25.85 C. The blood pressure remained at a high level until shortly before death. Associated

8. Johnson, G. S., and Blalock, A.: Experimental Shock: IX. A Study of the Effects of the Loss of Whole Blood, of Blood Plasma and of Red Blood Cells, Arch. Surg. **22**:626 (April) 1931. Blalock.[1]

with a slowing or cessation of the respiratory movements, the blood pressure rose and fell abruptly to zero. A rather marked increase in the concentration of the red blood cells was found.

In experiments in which whole blood equaling 1 per cent of the body weight was removed at one hour intervals from the femoral arteries of animals anesthetized by pentobarbital sodium and exposed to cold, the average period of survival was five hours and sixteen minutes; the average temperature at the time of death, 28.87 C. (83.97 F.), and the average quantity of blood removed, 4.86 per cent of the body weight. The decline in blood pressure was usually gradual rather than abrupt. In three experiments the terminal decline in blood pressure was abrupt, and a relatively small amount of blood had been withdrawn. Associated with the bleeding and the exposure to cold there was an increase in the concentration of the red blood cells. When the blood pressure reached a low level, a dilution usually occurred.

The results of the experiments in which exposure to cold and trauma were studied were variable. The average temperature at the time of death was 25.52 C. (77.94 F.). In some of the experiments, the difference in the weights of the traumatized and nontraumatized parts was sufficiently great to explain the cause of death on the basis of loss of local fluid alone. In these experiments there was a gradual decline in the blood pressure. In other experiments only a small part of the blood volume was lost into the injured extremity. The terminal decline in the blood pressure in these experiments was abrupt. The traumatization of the extremities was followed by an increase in the concentration of the red blood cells.

The results of experiments in which shock was produced during exposure to cold in animals anesthetized by morphine were quite different. Morphine alone was used as the anesthetic in the experiments on hemorrhage, while morphine supplemented by ether was used in those on trauma. The average loss of blood resulting in death in the experiments on hemorrhage was 6.38 per cent of the body weight or more than half of the total blood volume. The average loss of fluid into the injured extremity in the experiments on trauma was 4.58 per cent of the body weight. The average terminal temperature in the experiments on hemorrhage was 25.7 C. (78.3 F.) and in those of trauma, 19.7 C. (67.5 F.). The decline in the blood pressure in these experiments was gradual rather than abrupt.

It is to be noted from the experiments concerned with the influence of exposure to cold on the development of shock as a result of hemorrhage and of trauma that the results are dependent largely on the depth of anesthesia and the time of exposure.

Experiments were also performed in which the influence of the deprivation of food and water on shock produced by hemorrhage and by trauma was studied. Food and water were not allowed during the forty-eight hours preceding the beginning of the studies. The animals were anesthetized by barbital. It was observed that the loss of blood which resulted in the death of the animals was not much less than that found in experiments in which the animals were not deprived of food and water. The weight of the blood that was removed from the femoral artery in the experiments in which death was produced by bleeding was approximately the same as the difference in the weights of the injured and uninjured extremities in the experiments in which death was caused by trauma.

THERAPEUTIC USE OF CONCENTRATED ANTISTREPTOCOCCUS SERUM OF NEW YORK STATE DEPARTMENT OF HEALTH

IN CRYPTOGENIC STREPTOCOCCEMIA AND OSTEOMYELITIS OF CHILDREN

ADELE E. SHEPLAR, M.D.
MARTHA JANE SPENCE, M.A.
AND
WARD J. MacNEAL, M.D.
NEW YORK

In our series of twenty-six patients treated with the special concentrated antistreptococcus serum of the laboratory of the New York State Department of Health there were five patients with generalized or metastatic infection without a clinically recognizable entry portal. These patients were brought under observation in the hospital after invasion of the blood stream had taken place. It is uncertain whether the site of the initial invasion could or could not have been recognized at an earlier time by a competent observer. All five of these patients were children, aged 2 weeks, 27 months, 31 months, 43 months and 5 years, respectively.

REPORT OF CASES

CASE 1 (chart 1).—A. M., a boy, born on April 5, 1933, breast fed, had a high fever fourteen days after birth accompanied by swelling of the left thigh. On admission to the hospital five days later, on April 24, there was a marked swelling of the anterior portion of the left thigh with a slight excoriation in the inguinal folds on both sides. The left hip joint was immobile, and there appeared to be flaccid paralysis of the left knee and ankle. The entire limb was discolored by purple mottling. Aspiration of the swollen thigh on April 25 yielded about 2 cc. of bloody fluid from which hemolytic streptococci were obtained on culture. The next day the thigh was incised, but only a thin fluid was discovered. Roentgenologic study did not reveal any changes in the bone. On May 1 a blood culture was taken, and on the same day yellowish-brown pus was evacuated from a fluctuating swelling on the left buttock. This pus contained streptococci, and the blood culture yielded one colony of the same microbe per cubic centimeter of blood.

This work was made possible by a grant from the Josiah Macy Jr. Foundation.

From the Department of Pathology and Bacteriology, New York Post-Graduate Medical School and Hospital, Columbia University.

The patients whose records are utilized in this paper were treated in the clinical services of the following physicians: Dr. R. H. Dennett, Dr. A. G. De Sanctis, Dr. W. W. Lasher and Dr. M. C. Pease.

When growth in the blood culture had been recognized on May 3, a transfusion of 80 cc. was given, and 10,000 units of the concentrated serum of the New York State Department of Health was injected intramuscularly. The dose of serum was repeated on May 4 at 10 a. m. At this time the neck was stiff and the eyes glazed. An erysipelatous rash extended downward from the nose, and there were separate areas of it on the scalp and leg. Respiration became labored and the pulse irregular. Death occurred at 7:10 p. m. Necropsy revealed organizing subdural hemorrhage, probably from injury at birth, acute purulent meningitis, serous otitis media and mastoiditis. The heart valves were normal. The site of the original invasion was not recognized.

Case 2 (chart 2).—J. D. B., a boy, aged 27 months, became ill with fever on Feb. 25, 1933, and on March 1 there were vomiting and diarrhea. On March 2 a

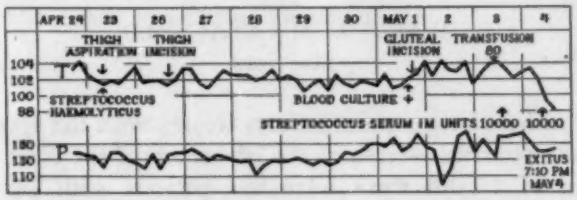

Chart 1.—Abridged clinical chart of A. M., a boy, aged 19 days. Apparently this baby had septicemia from the start. A positive blood culture was obtained on May 1, and the serum was administered on May 3 and 4. The child died on May 4.

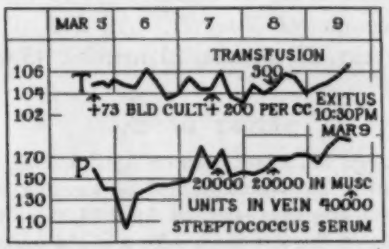

Chart 2.—Abridged clinical record of J. D. B., a boy, aged 27 months. This baby had a positive infection of the blood stream on admission. The serum was administered on March 7 and 8 intravenously and on March 9 by intramuscular injection. The child died on March 9.

maculopapular rash appeared, and this remained when the patient came to the hospital. On March 4 the temperature reached 106 F., and the child was admitted to the hospital on the following day. The urine showed protein (3+), and a systolic heart murmur was recognized. The eruption was in part purpuric. Blood culture taken at once on March 5 yielded 73 colonies of hemolytic streptococci per cubic centimeter of blood. When this result was recognized, on March 7, another blood culture was taken and one ampule (20,000 units) of concentrated streptococcus serum was injected intramuscularly. This dose was repeated the next day immediately after a transfusion of 300 cc. On March 9 an intravenous injection of two ampules (40,000 units) was given at 4 p. m. Signs of bronchopneumonia and of meningitis appeared, and the child died at 10:30 p. m.

Necropsy disclosed septic petechiae of the serous membranes, mucous membranes and skin, active vegetative mitral endocarditis, septic emboli in the myocardium and purulent infarcts of the spleen and kidneys. Examination of the head was not permitted.

CASE 3 (chart 3).—N. L., a boy, aged 31 months, has a longer record. He became ill on March 19, 1933, awakening during the night with severe pain in the right leg. Four days later the mother recognized swelling of the right foot and leg and a reddened area on the ankle. The temperature had ranged between 102 and 104 F. On March 24 the child was admitted to the hospital. At this time the swelling and inflammation of the right leg were more pronounced. The right forearm and wrist were also swollen and painful. The pharynx was bright red, and

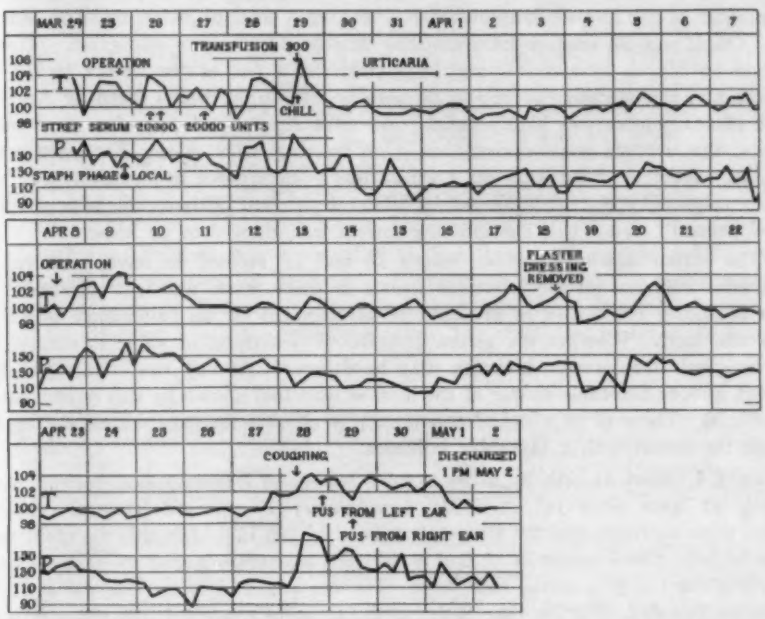
MAR 24 25 26 27 28 29 30 31 APR 1 2 3 4 5 6 7
OPERATION
TRANSFUSION 300
URTICARIA
CHILL
STREP SERUM 20000 20000 UNITS
STAPH PHAGE LOCAL
APR 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
OPERATION
PLASTER DRESSING REMOVED
APR 23 24 25 26 27 28 29 30 MAY 1 2
COUGHING
DISCHARGED 1 PM MAY 2
PUS FROM LEFT EAR
PUS FROM RIGHT EAR

Chart 3.—Abridged clinical record of M. L., a boy, aged 31 months. This child was operated on for osteomyelitis of the right arm and right leg on March 25. On the assumption that the infection was due to the staphylococcus, bacteriophage was applied immediately after the operation. The streptococcus serum was given on March 26 and March 27, the first dose subcutaneously and the second into the muscle. The patient did very well until April 27, when bilateral otitis media developed. The nature of the infecting microbe was not ascertained, but it is probable that the immunity to the streptococcus had disappeared during the period of one month.

the cervical lymph nodes were enlarged. Both ear drums were injected and slightly bulging.

The abridged clinical record is shown in chart 3. On March 25, at 6:30 p. m., pus was aspirated from the right ankle, and following this the right forearm and right leg were incised. In the forearm there was a deep abscess extending to the anterior surface of the pronator quadratus muscle but not involving the bones or

the wrist joint. In the leg there was erosion of periosteum at the lower end of the fibula, and the tibial periosteum was elevated with pus and small hemorrhages beneath it. An abscess containing about 120 cc. of pus extended about the right ankle, involving the tendon of the pronator longus muscle but not the joint cavity. Multiple openings were drilled in the lower end of the tibia, the periosteum was incised, and drainage of the soft tissues was established. Staphylococcus bacteriophage was at once applied as a wet dressing on the assumed diagnosis of staphylococcic osteomyelitis.

On the following day the microscopic and cultural examination of the specimens of exudate revealed the certain presence of hemolytic streptococci; staphylococci could not be recognized then or later. The child was therefore given 0.2 cc. of the concentrated streptococcus serum subcutaneously, and five hours later the remainder of the ampule intramuscularly, making a total of 20,000 units on March 26. On March 27 another intramuscular dose of 20,000 units was given. Transfusion on March 29 was followed by a chill and a rise in temparture to 106 F. There was a moderately severe serum rash on March 30, which faded by April 1. The clinical course was highly satisfactory until April 8, when, under ether anesthesia, the wounds were revised and Orr dressing with plaster bandages were applied. Another disturbance on April 27 was evidently due to an infection of the upper respiratory tract complicated by bilateral purulent otitis media, with streptococci present. When this subsided the patient was allowed to go home.

The serum administered on March 26 and 27 seemed to have exercised a beneficial influence on the infectious lesions in the forearm and leg. However, it was obviously inadequate to prevent the development of the respiratory infection a month later. Whether the serum contributed something of value in control of the original streptococcic infection may be debated. At any rate, one could not expect a more favorable course of the disease than that shown by this patient after March 30. Those of us who had opportunity to observe the patient were willing to credit the serum with a favorable influence.

Case 4 (chart 4).—D. S., a boy, aged 3 years and 7 months, had been ill with a cold at home since Jan. 4, 1932. On January 14 enlarged bilateral cervical nodes were observed, and the temperature reached 106 F. After this the child was kept in bed. On January 24 he had a chill, his temperature rose to 105.6 F., and he complained of pain in the right knee. He was admitted to the hospital at 4:30 p. m. on this day. At this time both ear drums were congested, the pharynx was red, and the cervical lymph nodes were firm and moderately enlarged. The child favored the right knee, but on physical examination it was found to be normal.

A blood culture taken at 8 p. m., January 24, revealed hemolytic streptococci after thirty-six hours. On January 25, because of some rigidity of the neck, limitation of movement of the right leg and the recognition of some problematic red spots on the skin, a spinal tap was done. This yielded a normal spinal fluid. Roentgenologic study disclosed capsular distention of the right hip joint on January 25 and of the right knee joint on January 27. Blood culture taken on January 26 was again positive. Transfusions were given on January 28 and 30. The spinal fluid was found to be infected with streptococci on January 28 and again on February 1. On this day the condition appeared desperate. The patient was unconscious, and there was slight general cyanosis. The concentrated antistreptococcus serum was administered, one ampule of 20,000 units into the spinal canal and a similar dose intravenously. Larger doses were administered on February 2 and 3. There was no evident response. The patient died early in the morning of February 4. Necropsy disclosed bilateral otitis media and mastoiditis,

bilateral purulent thrombosis of the lateral sinuses, diffuse purulent meningitis, bilateral cervical adenitis, bronchopneumonia and general sepsis.

Case 5 (chart 5).—C. M., a girl, aged 5 years, had an infection of the upper respiratory tract with cough and a rise in temperature to 102 F. in May 1933. At about this time she complained of pain in the left arm. Roentgenologic study at that time gave negative results. About a week later an abscess on the outer aspect of the left arm was incised, and a second roentgenologic examination in the following week disclosed changes in the upper portion of the humerus. On June 22 an operation was performed for osteomyelitis with pathologic fracture of the neck of the left humerus. On August 8 a roentgenogram revealed osteomyelitis of the entire shaft of the humerus, with apparent sequestration of the upper half. At this time the child was brought to New York.

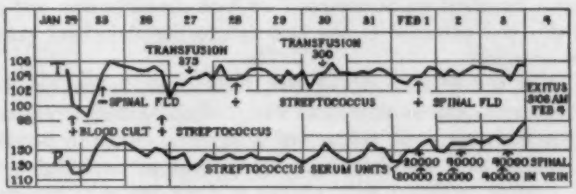

Chart 4.—Abridged clinical record of D. S., a boy, aged 3 years and 7 months. This child had an infection of the blood stream on admission to the hospital on January 24, and on January 28 the spinal fluid was found infected. Serum was given on February 1 and the following days. The child died early in the morning of February 4.

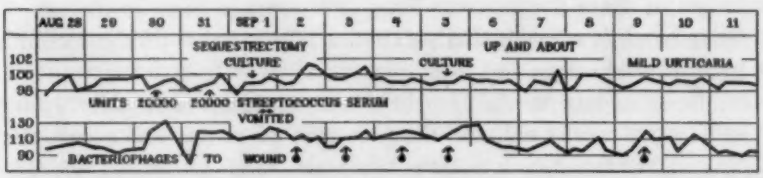

Chart 5.—Abridged clinical record of C. M., a girl, aged 5. This girl had osteomyelitis of the left humerus with sequestration. Serum was given intravenously for two days preceding the removal of the necrotic bone. The postoperative course was highly satisfactory, and the wound has gone on to complete healing without further incision. There was a moderate serum reaction in this case evident on September 9.

She was admitted to the Post-Graduate Hospital on August 17, at which time the upper half of the left arm was swollen, red and painful, with marked limitation of motion. There was a granulating incision on the outer aspect of the upper part of the left arm and also a draining left axillary sinus. Roentgenologic study at this time showed extensive old osteomyelitis involving almost the entire shaft of the humerus. The upper end of the old shaft was already separated as a sequestrum, with débris surrounding it. The middle and lower thirds of the old shaft appeared in the process of sequestration but not yet separated. A culture taken on August 18 from the draining sinus yielded pure growth of hemolytic streptococci. On August 21, a transfusion of 315 cc. was given, and the arm was immobilized

by a plaster dressing. It was deemed unwise to attempt sequestrectomy at this time because of the streptococcic infection, although the general condition of the patient was good.

A brief portion of the abridged clinical record is shown in chart 5. At the request of the surgical consultant, a preliminary treatment with streptococcus serum was undertaken in preparation for the operation. On August 30, a minute intracutaneous injection of the serum gave no evidence of hypersensitiveness. This was followed by a subcutaneous injection of 0.5 cc. of the serum and then after an hour by the intravenous injection of the remainder of the ampule making a total of 20,000 units for this day. On August 31 another ampule of 20,000 units was given intravenously. The sequestrectomy was performed on the following day with only slight disturbance to the patient. Her appetite was good on September 2, and on September 6, five days after the operation, she was up and about the ward. An itching erythema appeared on September 7 or 8 on the right arm and neck, and by September 9 this had extended to the face and to the abdominal skin, apparently a mild serum eruption.

Cultures from the exudate about the sequestrum, taken on September 1, yielded Staphylococcus aureus as well as streptococci. Subsequently other bacteria appeared in the drainage from the wound and sinus. On this account bacteriophages were applied as a wet dressing. The patient still remains under observation in good general condition with sinuses entirely healed. The point of chief interest for the present report has to do with the prophylactic use of the serum in preparation for surgical operation on a field infected with hemolytic streptococci.

COMMENT

Physicians who do not employ antistreptococcus serum will see in the record of these five patients little to encourage them in its use. On the other hand, it appears that a fair test of the value of the serum has not been afforded here.

In the first patient, A. M., the fever appeared on April 19, when the baby was 2 weeks old, and the first dose of serum was administered on May 3 after a blood culture taken on May 1 was recognized as positive. This was on the day before death, at a time when meningitis must have already been present, according to necropsy.

The second patient, J. D. B., became ill with fever on February 25, and the first administration of the serum occurred on March 7, when the blood culture taken two days before had shown positive growth. Necropsy on March 9 revealed an acute vegetative mitral endocarditis with associated septic complications.

The fourth patient, D. S., was ill from January 4, with a temperature of 106 F. on January 14. The serum treatment was initiated on February 1, eight days after the positive blood culture was taken on January 24 and four days after the recognition of meningitis on January 28.

The third patient, N. L., had been ill only since March 19. After the operation for osteomyelitis on March 25 the surgeon asked for the assistance of bacteriotherapy because of the impression that the disease was due to the staphylococcus. When the bacteriologic studies disclosed

the true etiology, the streptococcus serum was administered on March 26 and 27. There was a moderately severe serum rash four days later, but in other respects the behavior of the patient left little to be desired for nearly a month. One cannot be sure of the part played by the serum, but the record is at least suggestive. Apparently the protective effect of the serum had disappeared by April 27, or else the extension of infection into the ears was due to some unrelated organism. We are inclined, however, to believe that the continued frequent administration of small doses of the serum would have been a good thing in this case.

The fifth patient had already suppressed the original invasion of the blood stream. In her case the serum was employed as a safeguard against lighting up a streptococcic infection still persisting in the arm. The actual result was all that had been desired. Whether the patient would have done as well without the serum remains undetermined.

In our experience specific bacteriotherapeutic measures are most often instituted after too much delay. The first, second and fourth of these four patients represent examples. In the case of the third patient the earlier administration of the serum came about through a misapprehension. The bacteriologists were called in consultation in the hope of treating a staphylococcic infection with bacteriophage and once this contact with the patient had been made, the early administration of streptococcus serum became possible.

CONCLUSIONS

1. In vegetative endocarditis due to the hemolytic streptococcus and in meningitis coupled with bacteremia due to the same organism, the therapeutic use of antistreptococcus serum, in our hands, has not been successful.

2. The administration of the concentrated antistreptococcus serum of the New York State Department of Health in one case of streptococcic osteomyelitis was followed by a favorable course of the disease.

3. In a second patient with osteomyelitis the injection of the serum for two days preceding a sequestrectomy was followed by an unusually fortunate surgical result.

FIFTY-FIFTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

JOHN G. KUHNS, M.D.

EDWIN F. CAVE, M.D.

SUMNER M. ROBERTS, M.D.

AND

JOSEPH S. BARR, M.D.

BOSTON

JOSEPH A. FREIBERG, M.D.

CINCINNATI

JOSEPH E. MILGRAM, M.D.

NEW YORK

AND

ROBERT I. STIRLING, F.R.C.S. (EDIN.)

EDINBURGH, SCOTLAND

CONGENITAL DEFORMITIES AND DISTURBANCES OF GROWTH

Comparative Study of Congenital Coxa Vara and Coxa Plana.—Carnitz [1] made histologic examinations of three specimens from the femoral head in congenital coxa vara and compared these with the pathologic changes recorded in coxa plana. He concluded that, histologically, infantile coxa vara and coxa plana cannot be differentiated. They appear to be variations of the same developmental disturbance during growth.

Anatomic Basis and Origin of the Cross-Striations in the Metaphyses of Growing Bones.—Hamperl [2] studied the broad bands of cross-striation in growing bones resulting after intoxication from phosphorus, arsenic or lead and from syphilis and deficiency of vitamin D. He excluded from study the thin transverse lines which he observed in roentgenograms with each year of growth. A histologic examination of these broad metaphyseal bands was made in two cases. The bands consisted of a thick network of bony lamellae enclosing the remains of calcified cartilage. These bands apparently had formed at the epiphyseal line and on growth had moved out into the metaphysis. They resulted from a disturbance in enchondral ossification. No osteoclasts were seen in these areas. In mild cases the bands represented delayed absorp-

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This report of progress is based on a review of 213 articles selected from 467 titles appearing in medical publications approximately between April 1 and July 30, 1934. Only those which seemed to represent progress were chosen for review.

1. Carnitz, H.: Acta chir. Scandinav. **73**:521, 1934.
2. Hamperl, H.: Ztschr. f. Kinderh. **56**:324, 1934.

tion of the calcified cartilage ground substance. The approximate duration of the disturbance could be calculated by the distance of the band from the epiphysis, since in early life long bones such as the tibia grow about 3 mm. a month in summer and 2 mm. a month in winter.

[ED. NOTE.—These observations are interesting. In the experience of the editors, growth at the epiphyseal line is not as constant as this article suggests.]

DISTURBANCES IN OSSEOUS METABOLISM

Vitamin D Milk.—Wyman [3] stated that milk containing 432 U. S. P. revised units of vitamin D per quart (946 cc.) automatically prevents the occurrence of rickets. The milk should be given in the summer as well as in the winter in climates similar to that of New England. While 382 units amply supply the need for vitamins, milk of lesser potency may be adequate.

Kramer and Gittleman [4] reported that as little as 108 U. S. P. revised units of vitamin D per day produced a definite curative action in patients with rickets. With the amounts fed there was no difference in effectiveness between vitamin D milk prepared by direct irradiation and similar milk produced by feeding cows irradiated yeast.

Wilson [5] made a clinical study of the efficacy of milk fortified with 405 U. S. P. revised units of vitamin D per quart in the form of cod liver oil concentrate in preventing rickets. Thirty-three artificially fed infants (two thirds of them were Negro or Italian) were selected for study. Most of these were under 8 weeks of age in this period. Of the thirty-three, fourteen remained normal, slight rickets developed in seventeen and a moderate degree of rickets appeared in two. The conclusions were that since the amount of vitamin D necessary to prevent rickets is dependent on the rate of growth and since the rate of growth does not conform to the daily consumption of milk, fortified milk should contain enough vitamin D to afford protection when considerably less than a quart is consumed per day. Four hundred and five units per quart did not prove sufficient. How many units are necessary must be shown by future studies.

[ED. NOTE.—In the past few years many different ways of supplying vitamin D to infants have been proposed. Since they are all simpler than the administration of cod liver oil, there has been a tendency to adopt them too quickly. As the preceding articles show, the status of milk as a substitute for cod liver oil is not yet definitely known.]

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3. Wyman, E. T.: New England J. Med. **209**:889, 1933.
4. Kramer, B., and Gittleman, I. F.: New England J. Med. **209**:906, 1933.
5. Wilson, W. R.: Prevention of Rickets by Milk Fortified with Vitamin D (150 Steenbock Units of Vitamin D per Quart), J. A. M. A. **102**:1824 (June 2) 1934.

Hunger Osteopathy; Juvenile and Late Rickets.—From a clinical investigation, Crawford and Cuthbertson [6] concluded that the essential difference between the metabolism in a case of hunger osteopathy and one of rachitic condition was that the mineral salts were stored rapidly without the administration of irradiated ergosterol in the first case, whereas in the second irradiated ergosterol had to be added before an appreciable retention was secured. They considered that although hunger osteopathy and late rickets (osteomalacia) are not necessarily identical in their nutritional origin, both occur with a deficiency of vitamin D.

Calcium and Phosphorus Metabolism in Diseases of the Thyroparathyroid Apparatus.—From a careful investigation of cases of hyperthyroidism, Hansman and Wilson [7] concluded that a direct catabolic effect of thyroxine on the calcium deposits in bone, such as has been claimed to exist, cannot be the cause of the excessive mobilization and excretion of calcium and phosphorus. In a second paper, Hansman [8] concluded that the beneficial effect of the administration of vitamin D in cases of hypoparathyroidism is not due to better absorption of calcium or of organic phosphorus or of the product of calcium times phosphorus. He suggested that vitamin D acts by making the calcium available for tissue metabolism.

Relation of Thyroid, Suprarenal Glands and Islands of Langerhans to Malacic Diseases of Bone.—Golden and Abbott [9] stated that the evidence at hand indicated that skeletal decalcification of a degree sufficient to be of differential diagnostic importance on the roentgenogram and attributable to endocrine disturbances may be encountered in hyperthyroidism, but not in hypothyroidism, disease of the suprarenal glands or diabetes in adults. In diabetes in children decalcification of the bone was occasionally found, for which acidosis or malnutrition or both were probably responsible.

TUBERCULOSIS

Treatment of Surgical Tuberculosis with Splenic Extract.—After following under carefully controlled conditions twenty patients with surgical tuberculosis, ten of whom received splenic extract, Barr [10] concluded that there was insufficient evidence of a therapeutic effect of splenic extract on the course of surgical tuberculosis.

Tuberculosis of Shafts of Long Bones.—Van Gorder [11] reported six cases of tuberculosis of shafts of long bones in Chinese. The age ranged from 9 to 21 years. The clinical, pathologic and roentgenologic features

6. Crawford, A. M., and Cuthbertson, D. P.: Quart. J. Med. **3**:87, 1934.
7. Hansman, F. S., and Wilson, F. H.: M. J. Australia **1**:37, 1934.
8. Hansman, F. S.: M. J. Australia **1**:81, 1934.
9. Golden, R., and Abbott, H.: Am. J. Roentgenol. **30**:641, 1933.
10. Barr, J. S.: J. Bone & Joint Surg. **16**:173, 1934.
11. Van Gorder, G. W.: J. Bone & Joint Surg. **16**:269, 1934.

of the disease were discussed. The bones involved were: ulna (four cases); tibia (one case), and radius (one case). Five patients were cured by subperiosteal resection of the diseased bone. The sixth patient did not report for the study of the end-results but was presumably well.

POLIOMYELITIS

Poliomyelitis in California.—Apropos of the epidemic of anterior poliomyelitis in Los Angeles in June 1934, an editorial [12] in *The Journal of the American Medical Association* answered two questions, universally asked when the incidence of infantile paralysis is higher than normal: 1. Is it dangerous to travel through a district having a high incidence? There is a definite danger, particularly for children under 6 years of age. It is impossible to protect a child against contact, since the disease can presumably be distributed through carriers. This danger holds until the advent of really cool weather. 2. Should mass immunization of apparently well children be carried out? Neither whole blood nor convalescent serum has been used sufficiently in controlled experiments to provide data on this subject. If such experiments are made, accurate records should be kept so as to determine future practice.

Creatine-Creatinine Exchange in Poliomyelitis and Its Influence by Glycine.—Gross [13] determined the creatine-creatinine excretion in seven cases of poliomyelitis during the period of regeneration before and after the administration of glycine. The spontaneous high excretion of creatine bore a certain relationship to the severity of the disease. After the administration of from 15 to 20 Gm. of glycine a day, a definite increase in the excretion of creatinine in the urine was observed, while the amount of preformed creatine did not measurably change. The increase varied with the patient and with the amount of glycine administered. The appearance of extra creatininuria after the administration of glycine was not specific for muscular dystrophy. Gross suggested that daily doses might favorably influence the period of regeneration in poliomyelitis.

[ED. NOTE.—Various reports on the use of glycine to improve the muscular metabolism have appeared in the literature, a few of which have been reviewed in earlier reports of progress. The question of its therapeutic value in such conditions is still sub judice.]

CHRONIC ARTHRITIS

Autogenous Vaccines in Rheumatoid Arthritis.—Short and his co-workers [14] studied the action of autogenous vaccines in patients with chronic arthritis and in normal controls. They concluded that in arthritis

12. Poliomyelitis in California, editorial, J. A. M. A. **102**:2106 (June 23) 1934.
13. Gross, W.: Ztschr. f. klin. Med. **126**:152, 1934.
14. Short, C. I.; Dienes, L., and Bower, W.: Am. J. M. Sc. **187**:615, 1934.

there is no allergy to streptococci, as shown by skin reactions, comparable to that in certain other chronic infectious diseases. Skin tests did not permit a satisfactory selection of specific bacteria for vaccine therapy. Variations in the skin reactions were thought to be due to a difference in dermal irritability, to natural toxicity of certain bacterial species or to sensitization to certain bacterial groups. The authors expressed the belief that the therapeutic effect of autogenous vaccines was nonspecific.

Histologic Changes in the Knee Joint with Advancing Age; Relation to Degenerative Arthritis.—Parker and his colleagues [15] studied one hundred knee joints of elderly persons and found that the synovial membrane, the articular cartilage and the subchondral bone undergo certain changes with age comparable to degenerative or hypertrophic arthritis. In some cases hyaline cartilage showed the power to regenerate. The synovial membrane was normal except in those cases in which there was damage to the articular cartilage. Other changes in the cartilage and bone were described. The bony exostoses in traumatic joints were found to be due either to a projection of bone and cartilage over the surface of the joints or to a depression in the cartilage, thus giving the appearance of a bony outgrowth.

THE SPINE

Sciatica and the Sacro-Iliac Joint.—After performing anatomic studies on the relationship of the piriformis muscle, the sacro-iliac joint and the sciatic nerve, Freiberg and Vinke [16] found that prolonged spasm of the piriformis muscle may produce circulatory disturbances in the sciatic nerve. These disturbances in time produce adhesions between the sciatic nerve and the piriformis muscle, especially as in many instances the sciatic nerve passes through the belly of the piriformis muscle. On this basis, the relief from sciatic pain following manipulative measures may be explained on the basis of the release of adhesion between the piriformis muscle and the sciatic nerve and the stretching of a contractured piriformis muscle. The authors did not attempt to explain all sciatic pain on this basis.

Relaxation of the Pelvic Joints in Pregnancy.—According to Abramson and his co-workers,[17] relaxation of the pelvic joints is a normal physiologic process beginning in the first half of pregnancy and affected little by parturition. In their patients the return to normal was

15. Parker, F., Jr.; Keefer, C. S.; Myers, W. K., and Irwin, R. L.: Histologic Changes in Knee Joint with Advancing Age: Relation to Degenerative Arthritis, Arch. Path. **17**:516 (April) 1934.

16. Freiberg, A. H., and Vinke, T. H.: J. Bone & Joint Surg. **16**:126, 1934.

17. Abramson, D.; Roberts, S. M., and Wilson, P. D.: Surg., Gynec. & Obst. **58**:595, 1934.

usually complete in from three to five months post partum. An abnormal relaxation was found in 25 per cent of the patients examined. The authors advised treatment with a pelvic sling during recumbency and with a sacro-iliac belt during the ambulatory stage. They stressed the importance of treatment to prevent late symptoms of strain of the pelvic joints.

Oblique View for the Demonstration of the Articular Facets in Cases of Lumbosacral Backache and Sciatic Pain.—Ghormley and Kirklin [18] described in detail their technic for taking oblique views of the lumbosacral region. They stated that these views gave them an opportunity to study in detail the articular facets of the weak back in the lower part of the lumbar region. They emphasized the importance of the facets in the production of pain in the lower part of the back and sciatic pain. The transverse axis of the pelvis is tilted at an angle of 32 degrees to the film, and an anteroposterior roentgenogram is taken. The tube is centered perpendicularly to the film, directly above the midpoint of Poupart's ligament on the elevated side.

The Lumbosacral Junction.—Mitchell [19] discussed the lumbosacral junction, its anatomy and physiology and certain defects in this region accounting for disability of the lower part of the back. He described a method of accurately measuring the lumbosacral angle. The article furnishes an excellent review of the subject and is well worth preservation as a reference to the anatomy and function of the lumbosacral junction.

Lateral Tilt of the Pelvis in Children.—That lateral tilt of the pelvis is sometimes due to a primary malrotation of the fifth lumbar vertebra on the sacrum was stated by Cyriax.[20] The condition is more common in females and is caused by a sudden twist of the trunk, as while playing games, or by actual trauma. The rotary movement of the spine is checked by the inertia of the pelvis at the lumbosacral joint. If the joint is not strong enough or is caught unawares, a rotary displacement of the fifth lumbar vertebra on the sacrum ensues. Immediate replacement may occur or the displacement may persist. In the latter case one side of the pelvis is tilted downward and forward and can be straightened only by the development of lumbar scoliosis. Treatment is by derotation without anesthesia. After-treatment consists of exercises if a weakness of the muscles or an actual scoliosis exists.

CIRCULATORY DISTURBANCES OF THE EXTREMITIES

Effect of Alternate Suction and Pressure on Blood Flow to the Lower Extremities.—In carefully carried out experiments Landis and

18. Ghormley, R. K., and Kirklin, B. R.: Am. J. Roentgenol. **31**:173, 1934.
19. Mitchell, G. A. G.: J. Bone & Joint Surg. **16**:235, 1934.
20. Cyriax, E.: Brit. J. Child. Dis. **30**:274, 1933.

Gibbon [21] found that alternating pressure and suction applied to an extremity definitely increase the peripheral blood flow to the extremity in spite of advanced organic disturbance.

Vasodilatation of the Extremities.—In considering peripheral vascular disease it is becoming increasingly important to differentiate clearly between organic occlusion of the vessels and vascular spasm, according to an editorial in *The Journal of the American Medical Association.*[22] The several tests used to determine peripheral vasodilatation are similar in principle, all employing thermo-electric measurements of the surface temperature. The procedures used have not been simple and all have had their contraindications. In 1933, however, an exceedingly simple method of producing vasodilatation was investigated by Gibbon and Landis.[23] They observed that immersing the forearms and hands in warm water produces vasodilatation in the lower extremities. Immersion for a half-hour is sometimes necessary, but even so the method is much simpler than the injection of foreign protein or the induction of spinal or general anesthesia. In every instance in which it was applied to a normal subject the surface temperature exceeded 88.7 F., which is the minimum response to anesthesia. This method was checked with the older, more complicated procedures, and similar results were obtained in normal persons and persons with a pathologic condition. Another promising procedure is the study of the peripheral pulse volume. Such a study can be made with the plethysmometer described by Scupham and Johnson.[24] The movement records the pulse volume wave graphically, so that it can be kept as a permanent record.

21. Landis, E. M., and Gibbon, J. H., Jr.: J. Clin. Investigation **12**:925, 1933.

22. Vasodilatation of the Extremities, editorial, J. A. M. A. **102**:932 (March 24) 1934.

23. Gibbon, J. H., Jr., and Landis, E. M.: J. Clin. Investigation **11**:1019, 1932.

24. Scupham, G. W., and Johnson, C. A.: Peripheral Vascular Phenomena: Peripheral Pulse Volume in Occlusive Arterial Diseases, Arch. Int. Med. **52**:877 (Dec.) 1933.

(*To be concluded*)

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